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AMERICAN JOURNAL of PHARMACY

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A Record of the Progress of Pharmacy and the Allied Sciences

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EDITORIAL

THE CHANGING MEANINGS OF WORDS.

Words are expressions of human thought and as thought develops and civilization advances, words increase in number and often change in meaning so as to better express thought. In brief, words develop as human beings develop—the words of yesterday may be quite different in meaning from the words of today. This is especially true of scientific and technical terms. As science and art develop its language develops and becomes more accurately expressive.

Take, for example, certain words of the sciences and art in which we are particularly interested.

The word drug is probably derived from the Anglo-Saxon word *drugan*, meaning "to dry," and was formerly applied to vegetable drugs only, because fresh vegetable drugs had to be dried before they could be used; the word chemical was formerly and is applied to chemical compounds only. Today the word drug is applied to "any substance having medicinal properties," whether of animal, vegetable or chemical origin. Thus, we have the various State and Federal drugs acts covering all kinds of medicinal substances.

Botany (Gr. *botane*, a plant, from *boskein*, to feed, graze) is the science which treats of plants. It was formerly regarded as a distinct science; today it is being regarded as a sub-division of biology (Fr. *biologie*, biology, from Gr. *bios*, life, and *logos* description), "the science of life," or "the science which treats of animals and plants with relation to their structure, function, origin or development, and distribution."

Materia medica (L. *materia*, material, and *medica*, f. of *medicus*, medical), or "drugs," formerly related to "the material from which medicines are made, or the substances and combinations used in medical practice, including explanations of the nature and effects of

medicines." Today it applies to "the origin or preparation, properties, action and uses of drugs." A dispensatory is practically an encyclopedia of materia medica, a pharmaceutical codex is a digest of a dispensatory, and a pharmacopœia is an official standard for the identity, purity, quality and strength of drugs.

Pharmacognosy (Gr. *pharmakon,* drug, and *gnosis,* knowledge) treats of "the identification, preservation and valuation of crude animal and vegetable drugs."

Pharmacology (Gr. *pharmakon,* drug, and *legein,* to speak) or "the science of drugs," formerly embraced all the drug sciences; today it is used largely as a substitute for pharmacodynamics (Gr. *pharmakon,* drug, and *dynamis,* power) which relates to "the physiological action of drugs," in contradistinction to therapeutics (Gr. *therapeutikos,* from *therapeuein,* to nurse, serve or cure), which relates to "the pathological action of drugs." Thus, we have the section on pharmacology and therapeutics of the American Medical Association.

Pharmacy (Gr. *pharmakon,* drug) embraces all the drug sciences, but specifically it relates to the practice of pharmacy, or "the science and art of preparing, preserving, compounding and dispensing drugs," or to "a drug store." In an analogous manner, medicine embraces all the medical sciences, but specifically relates to the practice of medicine, or the science and art of preventing, curing and relieving disease.

These thoughts are suggested by the address of former President Ambrose Hunsberger before the 1922 Convention of the National Association of Retail Druggists at Detroit, in which he said that:

"While it is everywhere acknowledged that not one of the branches of legitimate pharmacy has even a remote connection with the illicit distribution of habit-forming drugs, there is nevertheless a psychological connection established which associates in a more or less vague manner the retail drug store with newspaper reports of 'drug raids,' 'drug fiends,' and 'drug peddlers' in the mind of the lay reader. Efforts are being made to have newspapers use with the word 'drug' the qualifying term 'narcotic,' or else to drop the word 'drug' altogether and substitute the slang term 'dope.'

"This campaign has met with success in some instances and in others objection was raised to the qualifying term 'narcotic' as being too long for headline use, and to the word 'dope' because of the fact that it is slang. The latter objection seems unwarranted in the light

of the language that appears in most of the newspapers of the day and it is suggested that our members take advantage of every opportunity to encourage their local newspapers to make use of either the qualifying term or the word 'dope.' Constant usage will eventually add this word to our language, rendering the use of a confusing term unnecessary."

Efforts are now being made throughout the country to correct the injustice done to the drug trade by the misuse of the word drug by newspapers and magazines in place of the words narcotic and dope; and these efforts should have the most active support of all those associated with the manufacture, sale, distribution and use of drug-store products, because if the misuse of the word is not corrected, it will seriously injure the standing of the legitimate drug and pharmaceutical interests in the estimation of the general public.

Therefore, the newspaper and magazine world should be most strongly urged to employ the word "dope" instead of "drug" or "narcotic" as suggested by Mr. Hunsberger, in referring to dope users, dope peddlers, dope sellers, dope smugglers, dope ring, etc., because, while the word drug means "any substance having medicinal properties," a narcotic (Gr. *narkotikos,* from *narkoun,* to benumb, from *narke,* numbness, stupor), is "a drug that allays pain and induces sleep or stupor. It may stimulate emotion or intellectual activity, and in large doses it depresses the vital functions and may cause death," and a dope (D. *doop,* sauce, dip, baptism, from *doopen,* to dip, baptize, from *diep,* deep), is "a narcotic used for emotional or intellectual stimulation; the word being employed colloquially for any narcotic used by a habitue" (Fr., properly pp. of *habituer,* to accustom). Up to the present, the word dope has been used to express a variety of meanings—"any stupefying compound" (slang), or "any preparation of a thick, liquid or pasty character; or any greasy compound used as a lubricant, as axle grease"; or "any absorbent material, such as cotton, waste, sawdust, etc., used to hold lubricants," etc.

If the word dope is consistently and persistently used by newspapers and magazines in place of drug and narcotic, as suggested, it will soon come to have a definite and specific meaning and become a part of the common language, expressing only one thing—a narcotic used for emotional or intellectual stimulation, while the words drug and narcotic will retain their original and proper significations.

J. W. ENGLAND.

THE STORY OF EAU DE COLOGNE.

A recent issue of the Belgian *Journal of Pharmacy* contained an account by J. J. Hofmann of the development of the manufacture of Cologne water, an abstract of which appears in the *Schweiz. Apoth. Zeit.* (1923, v. 61, 409). The employment of odoriferous substances by solution or by diffusion in the air dates from the earliest historical period. The use of the fumes of burning sulphur as a deodorizer and disinfectant is mentioned in the "Odyssey." In many cases these odors were supposed to be acceptable to the divinities or to drive away evil spirits. They were also used to correct disagreeable bodily odors, and this was so extensive that it is likely that the table of the Roman lady of fashion was as well supplied with such articles as is that of her present-day representative. It was not entirely an error to attribute to these perfumes some disinfecting power, for we know now that essential oils have some restraining action on the development of microbes. As a rule, however, these actions are slight, and the service performed by washes, dentifrices and similar applications is not very great. In French history, the career of the "four thieves" is well known. They made a practice of robbing the dead and wounded on the battlefield, and, notwithstanding the frequency of contagious diseases, escaped infection. It is stated that the secret was that they drenched the exposed parts of their bodies with a solution of aromatic herbs in vinegar. It is to this fact that we owe the introduction into pharmacy of certain aromatic vinegars, especially that originally known as "four thieves vinegar."

For several centuries methods of distillation with water have been practised to obtain perfumed solutions from roses, orange flowers and similar materials. In the fifteenth and sixteenth centuries it was the custom in high society to wash the hands before and after meals in rose water. Such a practise was all the more advisable at that time, since the use of forks was introduced first (in Italy) in the fifteenth century, and into France and England much later. The use of orange flowers as a perfume began in the sixteenth century. They were employed in England as a protection against plague; in France as a perfume under the name "Water of Nafe," presumably from the Arabic "Nafah," "odorous." The water of orange flowers and the essence were made fashionable by the Duchess of Arzine, Princess of Nerolo, hence the term essence of Neroli.

It is not possible to fix the exact date when the distillation of essential oils with alcohol or their direct solution therein began. Alcohol was recognized as an active ingredient in fermented beverages, and as being capable of extraction by boiling, long before its definite character was determined. In fact the word originally meant a painting material, subsequently any finely divided substance, and, as late as the first decade of the nineteenth century, Davy spoke of the "alcohol of sulphur," meaning probably the precipitated form. According to the Belgian writer, the first perfumed liquid prepared by means of alcohol was "Hungary water," the legend concerning which is that a recluse gave to Queen Elizabeth of Hungary the formula for its preparation, and she used it with such marvelous effect that the King of Poland was hopelessly smitten and proposed to her. This perfume was obtained by distilling rosemary. In a work on perfumes published in Paris in 1765, the method of preparation, which is somewhat complicated, is described.

The vogue of the Hungary water was soon surpassed by that of Cologne water, and the latter has maintained its lead up to the present. Although first offered in commerce in Cologne, the evidence is that the inventors were members of an Italian family who resided near the Cathedral, and began their work in the seventeenth century. The family name was "Farina." The success of the manufacture led others of the name, or who assumed it, to enter the business, and the "Farinas" became numerous, although we need not believe the statement that every male child born in Cologne is baptized "Jean Maria Farina" in order that when he reaches the proper age he may manufacture genuine Farina cologne. Nor is it likely that the modern city, under the advanced systems of sanitation, deserves the criticism of Coleridge:

> "I counted two and seventy stenches,
> All well defined, and several stinks."

The Farina establishments are, of course among the sights of the city. The German guide will show you the Cathedral and say, "This is so high that I cannot tell you how high it is, but if you want some 'O de Colong,' come with me opposite." The Italian origin of the "water" is undoubted. The fact is shown by the formulas, and by the use of citrus products. In the sixteenth century some Italian convents cultivated the art of making perfumed waters, and even into the nineteenth century, the Convent of St.

Maria Novella in Florence was well known for this manufacture. In Cologne today is a firm, "Maria Clementina Klosterfrau," engaged in such manufacture.

HENRY LEFFMANN.

ORIGINAL ARTICLES

LIGATURES AND SUTURES.

By Dr. Fred B. Kilmer, Ph. M.; G. S. Mathey, Ph. G., Ch. G., B. C., and H. J. Dobbs.

This is the second of a series of papers discussing the subject of Ligatures and Sutures from a pharmaceutical standpoint. While in many respects elementary and incomplete, it is hoped that its publication may assist the pharmacist in handling this class of material.

A CHEMICAL STUDY OF CATGUT.

Many interesting and unsolved problems confront us in any attempt to study catgut from a chemical point of view. Catgut is a most complex albuminoid substance; an organized collagen or gelatin.

Omitting the details of the processes employed, the following results have been arrived at in the examination of samples of untreated catgut in our laboratory:

Approximate Analysis of Catgut.

Moisture at 105° C.	12.20
Total Solids (105° C.)	87.80
Alcoholic Extract (resins and waxes)	1.47
Chloroform Extract (wax and fat)	1.36
Benzine Extract (fats and waxes)	1.65
Aqueous Extract (coloring matter)	0.99
Ether Extract (fats and waxes)	2.20
Collagen convertible to gelatin	72.25
Proteids and Albuminoids not convertible into gelatin	9.43

(The benzine, chloroform, ether and alcoholic extraction figures represent extractions of separate lots of catgut.)

Inorganic Constituents.

Ash	2.03
Sulphur	1.20

Ash constituents: Phosphates, chlorides, sulphates, sodium, magnesium, calcium, iron.

Constituents of Catgut.

The foregoing rather rough analysis of catgut, together with a knowledge of the constituents of such an animal tissue, present some interesting problems in physiological chemistry.

Catgut is defined by the physiological chemist as a "colloidal substance" known as collagen, or the parent substance of glue and gelatin.

Of the eighty known chemical elements, fourteen or more have been found to be present in such a tissue as catgut. Here is a list of some of these elements:

Hydrogen, carbon, oxygen, nitrogen (these combined with sulphur form all animal proteins), phosphorus, sulphur, potassium, magnesium, calcium, iron, sodium, chlorine, manganese.

We have no conception, and no method of analysis now known can give us a knowledge of the way these elements are combined in such a tissue as catgut. The elements named as probably present in catgut are, of course, in the form of colloidal compounds—albuminoids, proteids, fats, etc. In the foregoing table we have over 70 per cent. collagen, approximately 10 per cent. of proteids not convertible into gelatin, with about 2 per cent. of carbohydrates, waxes, fats, etc.

Any analysis like the foregoing gives but little insight into the nature of collagen. Some idea of its chemical makeup may be gained by a study of the products of its near relative gelatin, which, on hydrolysis with hydrochloric acid (Kossel), yields the following substances: Lysin, glycin, alanin, phenylalanin, leucin, aspartic acid, glutaric acid, histidin, arginin, pyrolin, oxyprolin.

These may be considered as the degradation products, or products of the disintegration of the larger molecule. At least we do not know that they exist as such in collagen or gelatin.

From the point of physiological chemistry, catgut tissue belongs to that group of substances known as Proteins, specifically

to the sub-group known as Albuminoids (or Scleroproteins). It is a jelly-forming albuminoid, quite akin to gelatin or glue.

Collagen cannot be considered as a definite chemical compound, or a distinct chemical entity; its structural formula cannot be written out on paper, or, as one authority says of gelatin and other similar compounds, "it has a coarser physical, as well as a finer chemical, structure." It is a colloidal substance. Professor Prescott has stated in discussing the reactions in colloidal chemistry that there is "a chemical action within the molecules and a physical action between the molecules; they grade off into each other."

Something about the chemical and physical structure of gelatin is known, but we have only a limited knowledge as to collagen.

From what has been said as to the nature and constituents of catgut, we can form some idea as to what may happen in its manipulation and preparation for surgery. If we immerse catgut in water for an extended period, especially if we boil it, if we add acid or alkali, we start a train of action that may be far-reaching. Any chemical substance we may add, even such simple substance as common salt, will have its effect.

Taking up a few of the substances which have been, or are now, used in the preparation of catgut for surgery, we find that tannic acid and mercuric chloride act upon collagen so that it is more or less rendered unconvertible into gelatin. Chromic acid, formaldehyde and alum likewise produce a tanning effect, rendering the substance more or less unconvertible. These substances, as well as potassium permanganate, carbolic acid, and indeed all acids in some degree, act upon collagen, lessening its flexibility and rendering the substance brittle and weak.

Alcohol abstracts a portion of the fat and the water from catgut, and produces a contraction of the cells (coagulating the albumen), in this action a slight hardening being produced.

We can readily comprehend that watery fluids or steam are not suitable agents for the sterilization of catgut. In the application of dry heat collagen is unchanged, provided the catgut is absolutely free from moisture, but a fractional percentage of moisture is sufficient to act upon the collagen and the tissues are cooked and rendered brittle.

By the long-continued action of water (or moisture) col-

lagen is slowly converted into gelatin, and as catgut is hygroscopic, if stored in an atmosphere where moisture is present, there will be deterioration in proportion to the amount of moisture and the time of exposure.

Acid fluids act upon collagen very rapidly, so that in a slightly acid watery solution a portion of the collagen is at once changed.

The agents used in hardening catgut, such as chromic acid, alum, tannic acid, formaldehyde, etc., harden collagen so that it is changed slowly and absorption retarded.

The substances noted in the analysis under the term "Proteids and Albuminoids" differ from collagen in the fact that they are not convertible into gelatin by the action of boiling water.

Three forms of proteids seem to be present:

1. A body similar in some respects to collagen, but resistant to the action of boiling water.

2. Albumin and globulin bodies soluble in water, salt solutions, acids or alkalies, and rendered insoluble by boiling water.

3. Mucin, a form resistant to boiling water.

The proteids in the percentage present in catgut—9.43—have an influence upon the tensile strength and upon the absorbability of catgut. The proteids are acted upon by water, by the salts of mercury, tannic, chromic and other acids. The action of these agents is one of coagulation, by which they are rendered more or less insoluble and are hardened. The proteids in catgut are easily changed in the process of sterilization, where heat is employed and where moisture is present.

The proteids are also accompanied by their own ferment bodies, which in the presence of warmth and moisture convert them into peptone. The salts present in catgut exert little or no influence upon the tensile strength except that the age of the sheep and its condition when slaughtered influence the amount of matrix tissue.

From the foregoing it will be seen that an accurate knowledge of the chemical constituents of catgut is essential in order to meet the difficulties which may be encountered in its sterilization and preparation for surgical uses. It will also be apparent that when such a complex substance is embodied in a wound

tissue, after performing its office in holding the wound tissue together, it must be broken down, disintegrated, and taken up by the fluids in the body, and that herein begins another series of processes of absorbing interest to the surgeon, to the pharmaceutical and to the physiological chemist.

HARDENED CATGUT.

From the time of Lister many methods have been suggested for hardening catgut so that it will resist absorption.

Absorbable suture material can be treated so as to retard absorption when imbedded in the tissues. This can be brought about by acting upon catgut with chemical agents such as chromic acid and its salts, tannic acid, vegetable tannates, alum, formaldehyde, etc.

The action of the chemical used is of a nature akin to the one occurring in tanning hides for the production of leather, although it is never carried to the same degree of intensity. Thus the catgut so treated is not rendered unabsorbable. Otherwise, the finished material would remain unabsorbed in the tissues for a considerable period of time, acting as a foreign body, thereby causing discomfort to the patient and may even prove a source of infection.

Chromicizing Process.

The process generally in use is known as the chromicizing process. This consists of treating the catgut with a solution of chromic acid, or a solution of a salt of chromic acid. The object of treating catgut with chromic solution is to harden it so that its absorption is retarded to a certain degree only. Chromic catgut, therefore, has one great advantage in that it can be used in smaller sizes than is possible with plain gut, and under normal conditions its absorption will be slower.

In recent years a process has been devised whereby the intestinal tissues are chromicized in the soft, loose condition, before being twisted to make the strand. The strips of clean intestine are placed in the hardening solution, and under these circumstances it can be said that they are evenly treated throughout.

The strength of the chromicizing bath and the period of exposure depend upon the degree of hardness or resistance to absorption that is desired.

Time of Absorption.

Considerable confusion has arisen in the past through the terms used to describe hardened catgut. Very early in the use of the so-called chromic catgut the terms "ten," "twenty" and "thirty"-day were applied, as indicative of the time in which the strand would resist absorption. Animal tissue of this character is of such a nature that it cannot be treated by a hardening process that can be reduced to a time-table.

Chromicizing the intestinal tissue before twisting it to make a strand. This insures perfect evenness throughout.

Latterly catgut has been supplied in two grades of hardness, using the terms "medium-hard chromic" and "extra-hard chromic." These are purely relative terms, used to indicate the degree or rate of resistance that the catgut offers against absorption when imbedded in the tissues. It has been acknowledged by leading surgical authorities that these names are really more appropriate than the designation of "days."

It has been established that patients do not react alike, different tissues do not react alike, and that it is absolutely impos-

sible to prepare catgut which can be said to have any definite resistance than can be embraced in the exact term "days."

As indicating the relative value of these terms it may be stated that under ordinary conditions in the striated muscle, the material known as "medium-hard" chromic catgut, size No. 2, will retain its integrity for from ten to twenty days, whereas the "extra-hard" chromic catgut will retain its integrity for thirty to forty days, or perhaps slightly longer.

Time of Absorption Varies.

It must also be borne in mind that any of the terms which are applied to hardened catgut are relative only. For example, the use of the term "ten-day catgut" never meant that it would be absorbed in ten days.

This is perfectly obvious when one considers that in certain tissues the larger sizes of catgut, especially plain or unhardened catgut, may not be absorbed for a length of time much longer than ten days. It is also to be considered that a healthy man is apt to absorb catgut more quickly than a thin, delicate woman; that in tubercular and in anemic patients, particularly in the young or the very aged, absorption is apt to be slow. It is also to be considered that in what is known as the serous or mucous membranes, absorption is four times as quick as in the muscular tissue. Therefore the muscular tissue is taken as the standard of measurement.

It should also be remembered that the larger the strand the longer the absorption will be delayed. This is especially true of the knot. Hence, many surgeons use two small strands in the place of one large strand wherever possible, so as to avoid large knots that may lie in the tissue and later cause irritation.

While, in order to guide the physician, hardened catgut is labelled with the approximate number of days, it is more accurate and more satisfactory to disregard the days and to consider them in the terms "medium-hard" and "extra-hard." Thus the surgeon has every chance to select the right gut for the work he expects to do, according to his knowledge of the time necessary to have the strand remain in the tissue.

FORMER AND PRESENT-DAY METHODS OF PREPARING CATGUT.

Since the beginning of the modern era of surgery the number of methods which have been suggested for preparing catgut reach into hundreds. That the most of them have not been satisfactory is witnessed by the fact that they are no sooner suggested and tried than they are abandoned, and a new method offered by the author or promoter. Some of these methods are here explained for historical value only.

Listerian Methods.

The original methods of Lister were to immerse the catgut in solutions of carbolic acid, or to preserve it in juniper or other oils, and impregnate it with carbolic acid, corrosive sublimate, etc. Afterwards alcohol, either plain or in combination with antiseptics, was substituted for the juniper oil.

For the most part the Listerian methods of preparing catgut have long since been abandoned.

Hofmeister Process.

In this process the catgut was first hardened with formalin and then boiled in water for a few minutes. The action of the formalin is supposed to be sufficient to allow the catgut to be boiled in water, which would be impossible unless the catgut was hardened.

Boeckman Process.

The Boeckman process is a sterilization by dry heat. The authority recommended that the catgut should be impregnated with pyoktanin, placed in an envelope, and heated in an oven for three hours. It was found that if the catgut was heated at a temperature sufficiently high to effect sterilization, its tensile strength would be destroyed. As a matter of practice, heating in an oven was very irregular; that is to say, it would be one temperature at the top, another temperature at the center, and still another temperature at the lower part.

Von Bergmann Process.

In this process the catgut was placed in ether for six weeks, afterwards stored in bichloride alcohol for twenty-four hours,

and in turn transferred to ordinary alcohol. It has been found that the corrosive sublimate is here converted into an insoluble compound with the catgut tissue, and rendered inert.

Schimmelbusch Process.

This is an elaboration of the von Bergmann process, except that the catgut, after the ether, mercury and alcohol treatment, was kept in a solution of iodoform. It was found that the bichloride and the iodoform react upon each other, forming a compound highly irritating to the tissues.

Rice Process.

This is a process devised by the late Charles Rice, of New York, and consists of boiling the catgut in chloroform without pressure, after which it is boiled in alcohol and kept until used in a solution of biniodid of mercury in chloroform.

Bloch Process.

The raw catgut is cleaned in hot, soapy water, disinfected in a 5 per cent. carbolic acid solution and preserved in carbolized alcohol.

Roux Process.

Raw catgut is placed in a 2-1000 solution of bichloride for one hour, then in turpentine for eight days, removed and stored in alcohol.

Cartillet Process.

Raw catgut is exposed to a temperature of 140° C. (284° F.) in a glass vessel which is not hermetically closed, and stored in absolute alcohol.

Schuler Process.

Dry, raw catgut is placed in loose rings or coils in a wide-mouthed, open jar, covered with oil of lavender and exposed for half an hour to a temperature of 110° C. (230° F.) in a steam sterilizer.

Thiersch Process.

Catgut stored in juniper oil for twenty-four hours, then in glycerine for twenty-four hours, removed and preserved in absolute alcohol containing some juniper oil.

Fedorow Process.

Catgut macerated in ether for forty-eight hours, then in oil of turpentine for twenty-one days, then washed in ether and stored in 1-1000 bichloride in absolute alcohol.

Esmarch Process.

Commercial gut strings are well cleaned with a potassium soap (soft soap), then in clean water, wound on glass spools, placed for twelve hours in 1-1000 bichloride solution, then twelve hours in 1-2000 bichloride alcohol, removed and preserved dry in well-closed jars. Shortly before use it is soaked in 1-2000 bichloride alcohol.

Iodine Catgut.

Iodine catgut was introduced in 1901 by Prof. Claudius of Copenhagen. Originally it was made by storing the catgut in a watery iodine solution. This process resulted in a complete rotting of the catgut, and it was afterwards changed by Moszhowicz, who suggested the drying of the catgut after immersion in the watery solution of iodine.

Mann, of Buffalo, recommended the use of iodine in alcohol; other authorities have substituted chloroform.

Bartlett Process.

A St. Louis physician of this name devised a process of heating catgut in mineral oil, after which the gut was stored in an iodine solution made with refined methyl alcohol.

Home-Made and Hospital-Made Catgut.

Some hospitals attempt to sterilize the catgut which they use, believing this to be a matter of economy. This practice does not always work out satisfactorily. Owing to the multitude of duties, as well as the numerous changes in the staff of a hospital, coupled with a lack of understanding of the chemical nature of catgut and of the material of which sutures are made, there has resulted a great destruction of catgut, waste, infection, and a general lack of satisfaction.

Involved in the process of sterilization is not only the temperature employed, but the conditions under which it is applied.

For example, in the boiling of catgut in an oven there may be a difference between the temperature of the oven and the liquid of from fifty to seventy-five degrees.

Moreover, in the conditions just outlined, in taking the temperature of the liquid in which the catgut is boiled, it depends very materially upon the portion of the liquid in which the thermometer bulb is immersed. In other words, the lower or the uppermost strata of the liquid is apt to be better than the middle portion, unless the liquid be kept in constant circulation.

Quite universally it is found that in these processes when the heat is applied for a sufficient length of time to bring about the result desired, the material is so impaired in strength as to make it worthless, and not infrequently it is found not sterile when bacteriologically tested.

There are many other processes, too numerous to mention here. However, they are practically all based on combinations and modifications of those outlined above. Few of them produce a catgut that is both sterile and fit for use as a suturing agent.

Modern Sterilization.

The methods of sterilization and of handling ligature material in modern manufacturing laboratories are of a character which places them in the class of highly scientific, approved bacteriological procedures.

It must be remembered that different treatment is necessary for the different varieties of ligature material, and that no general process covers them all. However, certain prominent features are present in all processes, and the chief one that interests the surgeon is the Thermal Process.

In no case is it allowable for ligatures to be handled in a manufacturing establishment after sterilization has taken place; that is to say, unusual care in the handling must not be depended upon to keep the ligature sterile, but final sterilization must be carried out after the container is hermetically sealed.

Some makers of catgut have worked out elaborate and efficient processes such as cleansing and disinfection before the tissue is twisted to form the cord called catgut. Other manufacturers begin with the twisted strand of catgut, which, too

frequently, has not been prepared under clean and sanitary conditions. This condition would involve intricate problems to secure sterilization.

Modern methods involve a continuous series of processes, not dependent upon any isolated act, carried out along the following lines:

1. The cleansing and disinfection of the intestines directly after their removal from the sheep.

2. Disinfection of the individual ribbon. (Chromicizing can be carried out at this stage.)

3. Twisting the ribbon under sanitary conditions.

4. Dehydration and extraction under proper conditions to prevent injuring the material.

5. Heat sterilization applied in kind, quantity and manner to assure the effective destruction of all organisms, spore-bearing or non-spore-bearing, pathogenic or non-pathogenic, in short, any and all organisms that may be present.

It may not be out of place here to state that whatever variation occurs in the mode of heat application, it is necessary to reach and maintain a temperature of at least 305° F. This is essential to assure the destruction of all spore-forming organisms, thereby effecting sterility.

The consensus of opinion expressed by the leading bacteriological authorities is that there are some highly resistant spores requiring a temperature of 302° F. dry heat, maintained for one hour, for their certain destruction.

All organisms must be eliminated to bring about sterility. Organisms like the coccus, non-spore-forming bacillus and the vegetative form of spore-forming bacillus are destroyed at relatively low temperatures. However, when it comes to the spores it is a different matter. They have the property of being highly resistant to heat, some of them, like anthrax and tetanus, requiring long exposure at elevated temperatures.

6. Storing in proper fluid or envelopes and sealing.

7. Sterilizing after the tubes or envelopes are sealed.

8. To this should be added bacteriological examination of each lot for verification of sterility and control.

The best modern method combines a thorough continued disinfection or sterilization, not dependent upon any one feature, or upon the power of any antiseptic, or any one degree of heat, but upon the combination of the whole.

The Storing Medium.

Catgut is put up chiefly in tubes, and unless there is a needle with the catgut in the tube, chloroform is used as a storing medium, for the reason that it is necessary, if the tubes are to be boilable, to have in the tubes a liquid that is free from water. Chloroform also is very strongly germicidal, especially when heated. With catgut preliminary sterilization in hot oil is carried out, and after this treatment the catgut is put in tubes, covered with chloroform, and the tubes flame-sealed. Then they are subjected to sterilization by steam under pressure.

In the preparation of so-called non-boilable tubes the process is identical with the one described for boilable tubes, except that the chloroform is replaced by an alcoholic or other antiseptic solution; the tubes are then flame-sealed. These tubes cannot be submitted to sterilization by steam under pressure, as the alcohol contained therein would hydrolyze the catgut and convert it into gelatin, thereby rendering it unfit for use as a suturing material. All non-boilable catgut is, strictly speaking, an antiseptic rather than an aseptic suture.

With most other ligature material, such as silk, alcohol is used as a preserving medium, and the sterilization is also carried out after the tubes are flame-sealed, using steam under pressure for the purpose.

Many problems relating to the sterilization of catgut and its subsequent storage are still in the process of evolution. Much has been accomplished, but there still remains more to be done.

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A REVIEW OF THE METHODS FOR THE DETERMINATION OF ACETANILID.

By Edward S. Rose, Cedar Rapids, Iowa.

Some time ago the writer had occasion to determine the amount of acetanilid in some tablets concerning which the claim was made that the content was 10 per cent. less than that stated on the label. The method used was that outlined by Seidell [1] in which the aniline radical set free by strong acid is determined volumetrically with a potassium bromide-bromate solution. Using this method the acetanilid content was found to be only 2 per cent. less than that stated on the label instead of the 10 per cent. claimed, which result was finally accepted as correct. Because of this wide variation in results obtained, the writer decided to review this method along with others that have appeared in the literature and apply the most satisfactory ones in determining acetanilid as found mixed with other substances in tablets, pills, cachets, powders, and effervescing salts.

Part One.

PURPOSE—The several published methods for the determination of acetanilid were carried out using Acetanilid U. S. P. as material to work with in order to ascertain by comparison which method or methods were most satisfactory: first, as regards accuracy and dependability of uniform results; and second, the simplicity of manipulation and saving of time.

The chemicals used were of C. P. or U. S. P. quality.

Special reagents were prepared as follows:

Hydrochloric Acid—(a)—HCl (sp. gr. 1.19)—30 cc., H_2O qs 100 cc.

(b)—HCl (sp. gr. 1.19)—40 cc., H_2O qs 100 cc.

Bromine V. S. N/2—$KBrO_3$ 15 Gm., NaBr (or KBr)—250 Gm. H_2O qs 1000 cc.

Sulphuric Acid— (a)—H_2SO_4 (sp. gr. 1.84)—20 cc., H_2O qs 100 cc.

(b)—H_2SO_4 (sp. gr. 1.84)—8 cc., H_2O 40 cc.

(c)—H_2SO_4 (sp. gr. 1.84)—2 cc., H_2O qs 100 cc.

Sodium Hydroxide—NaOH-2 Gm., H_2O qs 100 cc.

EXPERIMENTAL WORK—

Method Number One—In this method by Seidell,[1] 0.15-0.3 gm. acetanilid was weighed in a 200 cc. Erlenmeyer, 40 cc. of HCl reagent (a) added, then boiled gently on a sand bath under a reflux condenser for 30 minutes, and titrated while hot with N/2 Br V. S. until a faint yellow color persisted. The author prepared this V. S. in another way by adding Br to an almost saturated aqueous solution of 50 gm. KOH until no more was absorbed, diluted somewhat to dissolve separated salts, heated to expel excess of Br, filtered, and finally water added to make 1 litre.

This method was easily and quickly carried out. The results obtained were in fact the finding of the acetanilid equivalent, which in practice is the factor of the V. S., and they were close and uniform varying within one-half of 1 per cent. The reaction is between the liberated Br and the aniline radical forming an insoluble tribromaniline. Six atoms Br react with one Aniline or Acetanilid. Primarily for convenience of reference this method is called the TRIBROMANILINE METHOD.

Method Number Two—In this the authors[2] direct that 1 gm. of acetanilid be saponified under a reflux condenser for 1½-2 hours with 3 gm. NaOH, 20 cc. alcohol, and 10 cc. water. The solution is transferred to a casserole on a water bath, the alcohol evaporated, and the residue then transferred to a separator and shaken out once with ether to remove the liberated aniline and the ethereal solution shaken out twice with water to recover traces of sodium acetate. The washings and original aqueous residue are transferred to a litre flask and 25 cc. of 85 per cent. H_3PO_4 added and connected to a condenser with a Kjeldahl bulb tube. The liberated acetic acid is distilled off in a current of steam until the distillate is neutral to litmus and then titrated with N/1 NaOH V. S. using Ph as indicator. One molecule of NaOH equals one of acetanilid.

In using this method careful attention was given to the several transfers and the setting up of the apparatus so as to prevent H_3PO_4 going over into the distillate and to prevent loss of the liberated acetic acid. From 6-7 hours' time was required for each determination. The results obtained, using the procedure as stated above except starting with a smaller amount of sample, were accurate within 1 per cent.

Method Number Three—This scheme of analysis by Emery [3] is given along with the determination of caffeine and consists of an hydrolysis with an acid; the removal of the caffeine with chloroform; then the addition of a slight excess of sodium bicarbonate; an acetylization and subsequent removal of the acetanilid with chloroform. The method was carried out with but slight variation as follows: 0.2-0.5 gm. acetanilid was weighed in a small Erlenmeyer, 20 cc. of HCl reagent (b) added and boiled gently under a reflux condenser for 30 minutes. The flask was cooled, the contents transferred to a separator with 10 cc. water and then shaken with three 40 cc. portions of chloroform which after clearing perfectly were discarded. The residue in the separator was treated with small portions of sodium bicarbonate until an excess was observed settling out. About 1 cc. acetic anhydride was added, shaken vigorously and allowed to stand a short time. The reformed acetanilid was removed by shaking in turn with four 25 cc. portions of chloroform. All of the chloroform was run through filter paper into a small weighed Erlenmeyer, the chloroform recovered, the flask disconnected and the remaining chloroform vapor blown out. Small portions of ether were added and evaporated by rotating the flask in a water bath. The flask was dried at 35-36° for 2-3 hours in an incubator, cooled in a dessicator and finally weighed. In the assay of acetanilid itself the shaking with chloroform after the hydrolysis is an unnecessary step but was carried out to show the efficiency of the method. Results were accurate within about 1 per cent.

Method Number Four—This method by Rose and Becker [4] is similar to Number Two in that the acetyl radical liberated as acetic acid is titrated with alkali V. S., however, it is more easily and quickly carried out since the acetanilid is hydrolyzed directly with a solution of sulphuric acid. The method was used as follows: 0.15-0.3 gm. of acetanilid was transferred to a 300 cc. round-bottomed flask with a long neck. Fifty cc. of H_2SO_4 reagent (a) were added, the flask placed on a sand bath at an angle to prevent loss by splashing and then connected with a distilling or Kjeldahl bulb tube to a condenser. Connections were made for distilling in a current of steam using boiled distilled water and the stopper sealed with a mash of ground flaxseed. Distillation was conducted somewhat slowly at first and enough heat was applied to the round-bottomed flask so as to keep the volume of liquid fairly constant. About 300 cc. of distillate were collected in a litre flask and titrated

with N/10 NaOH Ph. as indicator. Additional 25 cc. portions were collected and added to the flask and titrated until but a drop of V. S. was required to restore the pink color. Care was taken to avoid CO_2. A blank titration was run using about 300 cc. of boiled distilled water and allowance made accordingly.

One molecule of NaOH is equivalent to one of acetanilid. It required about two hours to carry out a determination. Results were accurate within one-half of 1 per cent. Primarily for convenience of reference further on this is termed the ACETYL RADICAL METHOD.

Method Number Five—In this the author, Mirkin,[5] directs that 1 gm. of acetanilid be boiled 4 hours with a mixture of 1 H_2SO_4 (1.84) and 5 of water. The writer used 48 cc. of H_2SO_4 reagent (b). Cool the solution and carefully neutralize with $NaHCO_3$, add HCl (6 mol. to 1 mol. aniline) and cool flask to —10° C. by throwing in pieces of ice and using a freezing mixture. Slowly add sodium nitrite solution, thoroughly shaking after each addition. From time to time test with potassium-iodide-starch paper which, by turning blue, should indicate the end of the reaction. The author states that it frequently happens that the test paper turns blue even when there is unchanged aniline, therefore near the end of the titration the analyst should wait several minutes after the addition of sodium nitrite solution before applying the test.

In this method the aniline radical is diazotized by the liberated nitrous acid. One part of $NaNO_2$ is equivalent to one of acetanilid. The writer followed the scheme as stated above using N/10 V. S. It required from 5-6 hours to complete a determination. To arrive at the exact end point was tedious and more or less uncertain. The results obtained were accurate within from 2-3 per cent.

Tabulation of Results.

	Acetanilid Found—Gms.				
Acetanilid	*Methods*				
Taken—Gms.	*No. 1*	*No. 2*	*No. 3*	*No. 4*	*No. 5*
0.150	0.1499			0.1491	
0.250	0.2498		0.2480	0.2496	0.2445
0.300	0.2991			0.3003	
0.500		0.5040	0.4966		0.5130
		0.5013	0.5000		
1.0					1.0070

Conclusions.

All of the methods, with the possible exception of Number Five, gave close uniform results.

Considering the accuracy of results along with the simplicity of manipulation and the saving of time, the writer found Methods One and Four called respectively TRIBROMANILINE and ACETYL RADICAL the most satisfactory. These names were primarily used for the convenience of reference, but being short and somewhat descriptive, they are suggested for adoption.

Part Two.

PURPOSE—

A vast number of preparations containing acetanilid put on the market in the form of tablets, pills, cachets, powders, and effervescing salts have a more or less general distribution over the country. Since the Federal and State Food and Drug Laws became effective officials have checked up in many instances the acetanilid content as compared with the statement on the package. Manufacturers of these preparations do or should occasionally check up the acetanilid content for their own satisfaction.

The Federal and State officials doubtless use the Tribromaniline Method (Number One, Part One) as it has been tentatively adopted by the Official Association of Agricultural Chemists. Emery [6] and his co-workers in the Bureau of Chemistry at Washington, who have done the most work on the analysis of preparations containing acetanilid, use this method. These investigators have in each case made a complete analysis of the principal ingredients.

The purpose of Part Two of this paper is to apply and to compare the usefulness of the Tribromaniline (Number One, Part One) and Acetyl Radical (Number Four, Part One) methods in the determination of the acetanilid in various preparations of a more or less complicated character.

MEDICINAL SUBSTANCES FOUND ALONG WITH ACETANILID—

According to the literature one or more of the following may be found with acetanilid in various preparations—aconite (alkaloids), aloin, antipyrine, arsenic, aspirin, codeine and salts (sulphate, phosphate), caffeine, cascarin, capsicum (and oleoresin),

cannabis, digitalis, gelsemium (alkaloids), hyoscyamus (alkaloids), heroin (and hydrochloride), ipecac (alkaloids), morphine (and sulphate), monobromated camphor, nux vomica (alkaloids), phenacetine (acetphenetidin), pyramidon, proponal, podophyllin, quinine and salts (sulphate, hydrochloride, hydrobromide), salol, sodium salicylate, sodium bromide, stramonium (alkaloids), sulphonal, trional, and veronal. Doubtless other substances than those mentioned may be found in combination with acetanilid. It is quite probable that many of these are rarely if ever found along with acetanilid in preparations that have a wide distribution; others may not now be used at all; the narcotic drugs that are subject to the Harrison Narcotic Act are now never found in preparations of this kind. It is probably the exception and not the rule that other antipyretics occur along with acetanilid. However, all of the list have been considered in the experimental work. Supplies of the narcotic drugs referred to just above were not available, so statements regarding them are taken from the general literature.

Qualitative tests for these different substances may be found in most text and reference books.

With these various preparations in the form of tablets, pills, cachets, powders, and effervescing salts the following amounts are suggested for analysis: In the case of powders and cachets 1 or 2 should be taken. An effervescing salt should be reduced to a fine powder and 0.4-1.0 gm. used. With tablets and pills, 10-12 should be weighed and reduced to a fine powder and 0.4-1.0 gm. taken. In all cases enough material should be used to contain about 0.150-0.3 gm. acetanilid for each determination.

Experimental Work.

CHLOROFORMIC EXTRACTION—

In the cases of mixtures the first step necessarily is an extraction with some solvent and chloroform is undoubtedly the best. Having tried the schemes of extracting on filter paper and in a small vial arranged as a percolator, the following procedure was finally adopted and used in all subsequent determinations since it could be quickly carried out and gave practically a complete extraction.

A portion of the sample finally powdered was weighed in a dry-lipped beaker. About 75 cc. of chloroform were added and stirred well and then filtered through paper into a 100 cc. flask

which had previously been graduated with chloroform and a 25 cc. pipette. Additional chloroform was added to rinse out the beaker, wash the lip of the beaker and filter paper, and finally the volume brought to the mark. Twenty-five cc. portions were transferred with a pipette to a suitable flask, the chloroform was recovered down to 2 or 3 cc., the flask then disconnected and while rotating it in a water bath the remaining chloroform vapor was quickly blown out with a pipette. The flask was cooled and the residue assayed by the respective method. If the sample to be assayed is of unknown composition, qualitative tests should be made with the residue of a few cc, of the chloroformic extraction to ascertain if substances of an interfering character are present.

Example of Procedure—1.0 gm. of an Acetanilid Compound Mixture consisting of acetanilid (50 per cent.), caffeine, sodium bicarbonate, powdered acacia, and milk sugar was extracted and 25 cc. portions put through both the Tribromaniline and Acetyl Radical methods. Caffeine was extracted by the chloroform, but it did not interfere with either method.

Tabulation of Results.

Acetanilid Present—Gms.	*Acetanilid Found—Gms.* *Tribromaniline Method*	*Acetyl Radical Method*
0.125	0.12349	0.1238
	0.1246	0.1255
0.250	0.2497	0.2485
	0.2475	0.24715

In subsequent references to "Acetanilid Compound Mixture" the one of the above compositon was used.

Of the substances enumerated under MEDICINAL SUBSTANCES FOUND ALONG WITH ACETANILID the following will be found at least to some extent in this chloroformic extraction: alkaloids (from aconite, gelsemium, hyoscyamus, ipecac, nux vomica, stramonium), antipyrine, aspirin, caffeine, codeine, heroin, morphine, monobromated camphor, pyramidon, proponal, podophyllin, phenacetine, quinine and salts, salol, salicylic acid, sulphonal, trional, veronal, and coloring and extractive matter from many sources. The usual excipients such as sugar, acacia, milk sugar, starch, etc., do not appear in this extraction.

Applying the Tribromaniline and Acetyl Radical Methods—

Of the substances removed by the chloroformic extraction the following were found to interfere with the general process of one or both methods and are conveniently placed in groups as:

(A) Alkaloids, Alkaloidal Salts (Heroin);
(B) Aspirin, Salicylic Acid, Salol;
(C) Antipyrine, Pyramidon, Coloring and Extractive Matter;
(D) Phenacetine.

All of these groups interfered with the Tribromaniline method while Heroin (group A) and groups (B) and (D) interfered with the Acetyl Radical method, therefore the following modifications were found necessary before submitting the chloroformic extraction to the general process:

(1) Group (A) was removed with weak H_2SO_4 solution.

Example of Procedure—A mixture of 1.0 gm. Acetanilid Compound Mixture and 0.3 gm. Quinine Hydrochloride was extracted with chloroform in the usual way to 100 cc. Sixty cc. were transferred to a separator and shaken thoroughly in turn with two 10 cc. portions of H_2SO_4 reagent (c), allowed to clear perfectly after each extraction before drawing off the chloroformic layer. About 3 cc. of this layer was evaporated to dryness and tested for alkaloids with Mayer's reagent. This treatment removed the Quinine Hydrochloride. The chloroformic layer was run through cotton and 50 cc. (equivalent to 0.250 gm. acetanilid) transferred with a pipette to a 200 cc. Erlenmeyer. The aqueous-acid residue was shaken with 30 cc. of chloroform, allowed to clear, run through cotton and 25 cc. of it added to the chloroformic extraction in the Erlenmeyer. The chloroform was recovered and the residue put through the general process of the Tribromaniline method.

Measured portions of the original 100 cc. chloroformic extraction were assayed by the Acetyl Radical method.

(2) Group (B) was removed by a saponification with NaOH solution.

Example of Procedure—A mixture of 1.0 gm. Acetanilid Compound Mixture and 0.250 gm. Salol was extracted in the usual way with chloroform using about 100 cc., all of which was collected in a 200 cc. Erlenmeyer. The chloroform was recovered

and 20 cc. of NaOH reagent added. The flask was rotated in a water bath for five minutes at 60-65° C., then cooled and 20 cc. chloroform added. The contents of the flask was transferred to a separator, then well shaken, allowed to clear and the chloroformic layer drawn off into another separator. Three more 20 cc. portions of chloroform were used in turn to extract the aqueous-acid residue being first used to rinse out the original flask. The combined chloroformic extraction was shaken with 25 cc. water and then drawn off through cotton into a 100 cc. flask. The wash water was shaken with 15 cc. chloroform, allowed to clear and the chloroformic layer drawn off through cotton into the above flask. Chloroform was added to the mark. Then 25 or 50 cc. portions (equivalent to 0.125-0.250 gm. acetanilid) were put through the general processes of the Tribromaniline and Acetyl Radical methods.

(3) Group (C) was removed by Method Number Three (Part One) modified.

Example of Procedure—A mixture of 1.0 gm. Acetanilid Compound Mixture and 0.3 gm. Antipyrine was extracted with chloroform in the usual way to 100 cc. Then the chloroform was recovered from a 50 cc. portion and the residue hydrolyzed in the usual way and transferred to a separator. Ten grams of sodium acetate were added and then shaken in turn with three 40 cc. portions of chloroform, allowing each extraction to clear perfectly, which was then drawn off and discarded. The antipyrine was entirely removed in this way, being salted out by the sodium acetate. The acid residue in the separator was treated with successive small portions of potassium bicarbonate, using a slight excess or in all about 10 grams. The acetanilid was reformed by the addition of about 1 cc. acetic anhydride or enough to make slightly acid, the mixture thoroughly shaken and allowed to stand about 15 minutes. After adding about 2 gm. potassium bicarbonate, or enough to make slightly alkaline, and agitating thoroughly, the acetanilid was removed by chloroform in the usual way using about 100 cc., all of which (equivalent to 0.250 gm. acetanilid) was put through the general process of the Tribromaniline method.

This group (C) did not interfere with the Acetyl Radical method so a 50 cc. portion of the original chloroformic extraction (equivalent to 0.250 gm. acetanilid) was assayed without modification.

(4) With group (D) all other substances present in the chloroformic extraction with the exception of acetanilid were removed so that it and the phenacetine could be weighed as a dried residue. According to the substances present modifications (1), (2), (3), were applied in their respective order. In practice any substance found in the chloroformic extraction and not classified under groups (A) and (B) will be removed by modification (3) such as caffeine, camphor monobromated, sulphonal, trional, veronal, etc.

Example of Procedure—A mixture of 2 gms. Acetanilid Compound Mixture, 1.0 gm. Phenacetine, 0.5 gm. Quinine Hydrobromide, 0.5 gm. Salol and 0.5 gm. Antipyrine was extracted in the usual way, using about 150 cc. chloroform which was collected in an Erlenmeyer. About 75 cc. of the chloroform were recovered and the remaining residue transferred to a 100 cc. flask and chloroform added to the mark, being used first to rinse out the Erlenmeyer. Then a 50 cc. portion was put through modifications (1), (2), (3), in the order as named, making a continuous process. In each modification the extraction with chloroform was collected in a flask such as was suitable for the succeeding modification and then in modification (3) the final extraction was made to 100 cc. At this point qualitative tests were made on the residues of 5 cc. portions of this chloroformic extraction for antipyrine, alkaloids, and salicylic acid (salol). Should any of these substances have been present it would have been necessary to resubmit a measured amount of the extraction to the respective modification. A 25 cc. portion was transferred with a pipette to a small weighed Erlenmeyer and the dried residue obtained as described in Method Number Three of Part One. This residue (equivalent to 0.125 gm. acetanilid and 0.125 gm. phenacetine) was put through the general process of the Acetyl Radical method. The result was expressed in percentage of Acetyl Radical (CH_3CO) carried to the second decimal place, using one molecule NaOH as equivalent to one of the Radical. Knowing the percentage of Acetyl Radical in both acetanilid and phenacetine as calculated from their forulas, the amount of acetanilid in the sample was readily found by alligation. Suppose for example the percentage of Acetyl Radical found was 27.93, for acetanilid it is 31.85 and for phenacetine 24.02, therefore by alligation every 3.91 parts in 7.83 parts of the dried residue is acetanilid.

Before using the Tribromaniline method the residue of a

25 cc. portion of the chloroformic extraction was put through the scheme of Emery [7] to precipitate the phenacetine as a periodide. For working details of this scheme the reader is referred to the original paper or Allen's *Commercial Organic Analysis,* vol. lx, page 472, or Fuller's *Chemistry and Analysis of Drugs and Medicines,* page 864. The precipitate was filtered off and an amount of the filtrate equal to 80 per cent. of the original residue (or equivalent to 0.1 gm. acetanilid) was transferred to a separator and enough sodium sulphite added to decolorize the remaining free iodine. Then about 0.5 cc. acetic anhydride and 25 gm. sodium acetate were added and the acetanilid removed with chloroform using three 50 cc. portions. The chloroformic extractions were collected in an Erlenmeyer, the chloroform recovered and the residue subjected to the general process of the method.

Whenever the statement is made that the volume was made to 100 cc. with chloroform the flask used had been previously graduated with chloroform and a 25 cc. pipette.

Tabulation of Results.

Acetanilid Found—Grams

Groups	*Acetanilid in sample assayed—Gms.*	*Tribromaniline Method with modification*	*Acetyl Radical Method with-*	*without modification*
(a)	0.250	0.249		0.2517
		0.2508		0.2513
		0.2525		
(b)	0.125	0.12486	0.1247	
		0.12317	0.1254	
		0.1238	0.1240	
		0.1243		
	0.250		0.2487	
(c)	0.250	0.24525		0.24784
		0.24747		0.25049
(d)	0.100	0.09887		
		0.09944		
	0.125		0.1225	
			0.1226	
			0.12399	

CONCLUSIONS—

The writer concludes that both the Tribromaniline and Acetyl Radical methods are useful to the analyst in the estimation of acetanilid when found in tablets, pills, powders, cachets, and effervescing salts. Both methods give good results.

When assaying preparations such as Compound Acetanilid Powder and those containing interfering substances which must be removed, either method may be used; however, the Tribromaniline can be carried out somewhat more quickly. The Acetyl Radical method may be carried out and the acid-aqueous residue while hot titrated with Br V. S. as in the Tribromaniline method, thus one method is made a check on the other.

With preparations containing in addition to acetanilid such substances as solid and powdered extracts alkaloids, alkaloidal salts, antipyrine, pyramidon, etc., the Acetyl Radical method can be used to a better advantage since it can be applied directly to the residue of the chloroformic extraction.

Where phenacetine is present with acetanilid the Emery procedure in which the phenacetine is removed as a periodide is perhaps the only method that has given good results. The use of the Acetyl Radical method and calculating the acetanilid by alligation is new. The results obtained might indicate that it is worthy of further consideration.

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WHAT IS A CHEMICAL?

By J. N. Taylor, M. S.[1]

There has recently come about a most interesting discussion regarding the definition of a synthetic organic chemical. According to *Chemical Age* (New York) for April, 1923, the Board of Governors of the Synthetic Organic Chemical Manufacturers' Association has adopted the following definition: "Synthetic Organic Chemical—An organic chemical which has been produced by a controlled process involving change in chemical identity." A "chemical" is defined as "a material containing a preponderating proportion of an individual substance of definite elementary composition." Attention was called to these definitions in an editorial appearing in *Chemistry and Industry* for May 18, 1923, and further reference was made to the definition of "synthetic organic chemical" by Mr. E. Parry in giving testimony at the hearing (June 15, 1923), on "Formaldehyde," under the Safeguarding of Industries Act (England) as to whether or not formaldehyde is a ***synthetic organic chemical.*** He observed[2] "that the difficulties of definition had become so great in the United States that only this month the Synthetic Organic Chemical Manufacturers' Association of the United States had attempted to define a synthetic organic chemical, but the definition arrived at was meaningless."

The subject of chemical nomenclature is one of general interest, engaging the attention of educators in the science as well as the various chemical societies and other associations having for their object the advancement of science. Some time ago the present writer took occasion to direct attention to the desirability of greater uniformity in chemical terminology,[3] especially in our schools and colleges. A number of welcome and helpful criticisms of the paper

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[2] "Chemistry and Industry." (*Jour. Soc. Chem. Ind.*) Vol. 42, No. 26, p. 643.

[3] Taylor, J. Norman: "Chemical Nomenclature and Pronunciation." *School Science and Mathematics,* Chicago, Vol. XX, No. 9 (1920). Reprinted in *Jour. American Pharm. Assoc.,* Philadelphia, Vol. 10, 10-11 (1921), and in *Chem. News,* London, Vol. 122, 7 (1921).

were received pointing out that the English language is a growing one, that it is yet in process of evolution and that growth and change in our language demand simpler and more concise forms for conveying chemical ideas. This is indeed true. In any live, growing language words change in meaning in the course of time. Couch, in his admirable series of articles now appearing in THIS JOURNAL, entitled "The Evolution of Chemical Terminology," traces this very interesting development of our science. Divergences in the connotation of a word or term, recognizably depend in great measure upon the aspect which the word or term assumes. Such terms as "chemical" and "synthetic organic chemical" for example, might each convey different meanings from the point of view of a manufacturer, a dealer, a teacher, or an analyst, or when viewed from the standpoint of the tariff or the census, or when thought of as entering into interstate commerce.

Certain words, when used in a legal sense, are specifically defined and the extent to which an adjective may partake of the attributes of the noun are, therefore, limited by definition. Certain Acts of Congress specify for the purposes of the Acts the limits in meanings of certain words. For example, the Food and Drugs Act, June 30, 1906, defines the term "drug" as used in the Act as "all medicines and preparations recognized in the U. S. Pharmacopœa or National Formulary for internal or external use, and any substance or mixture of substances intended to be used for the cure, mitigation or prevention of disease of either man or other animal." The noun "drug" and terms derived from it are, therefore, circumscribed in meaning when employed under the provisions of the Act. As another example may be mentioned the word "insecticide." The Insecticide Act of 1910, defines "insecticide" as follows: "The term 'insecticide' as used in this Act shall include any substance or mixture of substances intended to be used for preventing, destroying, repelling or mitigating any insects which may infest vegetation, man or any animals or households or be present in any environment whatsoever." Naturally, the adjective "insecticidal" is limited in meaning for the purpose of the Insecticide Act because of the meaning given the word "insecticide" by the framers of the Act. On the other hand, the *popular* meaning of words such as are noted above may extend beyond the limitations set down for them *ex cathedra*.

As an adjective, there appears to exist little, if any, confusion regarding the use of the term "chemical." We are accustomed to speak of "chemical reactions," "chemical compounds," "chemical products," etc., and, through custom and usage, their meanings carry no ambiguity. To what extent, however, may the popular concept of the meaning of the adjective be applied to the noun. When an attempt is made to distinguish between "chemical" and "chemical compound," between "chemical" and "drug," or between a chemical and the result of a chemical process, there appears to be a misunderstanding as to just what is conveyed when the word, "chemical" is employed as a noun.

It would seem apropos, therefore, in view of the present discussion of the meaning of the noun "chemical," to reaffirm the province of chemistry, hoping thereby to establish a position from which we can survey this question in the light of both theory and practice.

Chemistry investigates the composition and properties of substances and the changes which they undergo. It deals with the energy changes within and between or among molecules and atoms of substances. Hence, in its application, it includes all material things which are the result of energy *transformations*. To the chemist, therefore—and who should be better qualified to speak on chemical topics than the chemist—all substances which enter into and result from such energy transformations are chemicals.

There is nothing original in this statement, however. Munroe [4] as long ago as 1905, in his monograph "Chemicals and Allied Products," in discussing the classification of materials coming within the scope of the investigation for the Bureau of the Census declared that, *"in the strictest technical sense every material thing is a chemical."*

Obviously, until some such fundamental definition of a chemical is agreed upon and the start is made from this base, the efforts to obtain divisional definitions that will be generally accepted will be unavailing. With this in mind the foregoing definition is presented for consideration.

[4] Munroe, Charles E.: "Chemicals and Allied Products," Census of Manufactures: 1905, Bulletin 92, Bureau of the Census, Department of Commerce and Labor, Government Printing Office, Washington, 1908.

PROFESSOR ARNO VIEHOEVER.

The Chair of Biology and Pharmacognosy at the Philadelphia College of Pharmacy and Science is now filled by Arno Viehoever, recently of Washington. Thus comes to the College and to a Professorial Chair long held by a line of worthy and able men, another whose record as a searcher in the realms of science, as a worker in the ranks of pharmacy and as a profound scholar and thinker, brilliantly maintains the best traditions of this pioneer College. That Dr. Viehoever is indeed eminently fitted to the new position which he has elected to occupy is well substantiated in the following sketch of his career, as quoted largely from the pen picture by Prof. Stanford, appearing in a recent issue of *The Northwestern Druggist:*

"Arno Viehoever was born at Wiesbaden, Germany, in 1885. Tradition says that at the age of three he had classified the entire flora of Hesse-Nassau botanically, chemically, and physiologically. Neighboring mothers, having cause to fear the experimental mind of the future scientist, muttered that typically German incantation, 'Verboten!' when small Arno, his pockets bulging with suspicious vegetation, toddled over to invite their offspring out to play.

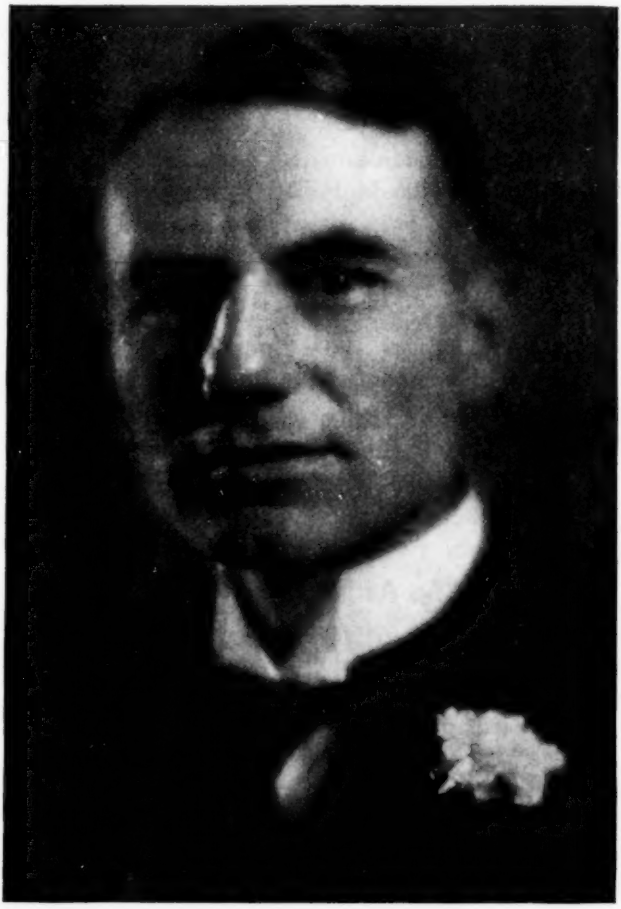
"The first authorized record of the scientific progress of our pharmacognosist begins at Munich. Here he studied under Baeyer, inventor of synthetic indigo, and Roentgen, of X-ray fame. Among his masters at the University of Marburg were Ernst Schmidt, the toxicologist, and Arthur Meyer, leading German pharmacognosist of his day. Under Meyer, whose assistant he later became, he did his major work, receiving his final degree, that of Doctor of Philosophy, with the distinction *magna cum laude*. During his university career he took several honors and prizes, among them the first prize and medal of the Hagen-Buch Endowment, and the prize of the University of Marburg.

"From Marburg he came, in 1914, to assume charge of the newly established Pharmacognosy Laboratory of the United States Bureau of Chemistry.

"Contributes Important Research Work.

"Since his arrival in this country, Dr. Viehoever, besides supervising the regulatory work whose nature has already been outlined, has found time to engage in and publish upon almost numberless botanical, chemical, and pharmacognostic themes. The pages of the *Journal of the American Pharmaceutical Association* have been

especially enriched by the pens of himself and his co-workers. In 1919, with C. O. Ewing, and J. F. Clevenger, he was awarded the Ebert prize of the A. Ph. A. for study of commercial viburnum barks and of the ash-content of American drugs, a research which dealt with methods of testing cleanliness in over 300 different products.



PROFESSOR ARNO VIEHOEVER.

"Other publications bearing his name have appeared in the *Journal of Agricultural Research,* the *Journal of Biological Chemistry,* and other scientific and technical journals. Among the wide range ot subjects may be mentioned a study of war-time mustard stubstitutes

and adulterants, an investigation of substances in the cotton plant which attract the boll-weevil, a study of the hellebores—important insecticides—and research in ipecac—nauseant subject—which may result in considerably cheapening and increasing the supply of that most expensive South American drug, around which so much therapeutic interest now centers, for it is our chief reliance in the treatment of pyorrhea and other amoebic diseases. Another study, undertaken just before the war, resulted in the exclusion from the United States of large cargoes of Oriental beans which much resembled the species sacred to Boston, but differed from that in being liberally seasoned by Nature with prussic acid. Some of these beans were to have been used for army consumption.

"The government standards for drugs under the Food and Drugs Act—the United States Pharmacopœia and National Formulary—require decennial revision to keep them abreast of clinical and scientific knowledge. So precise and exacting are some of these standards that the presence of two per cent. of browned or discolored leaves in digitalis is held to disqualify this important medicinal as a heart tonic. Besides these medicinal standards, the Department of Agriculture is empowered to impose its own criteria upon foods and spices which do come within the scope of the official books. In revision work and in the evolution of the departmental standards the Pharmacognosy Laboratory has had a most active part.

"An Active Collaborator.

"Dr. Viehoever has not contented himself with being a mere laboratory chief. Through co-operation with the Bureau of Plant Industry he surverises the culture of many of the plants under his investigations, particularly those whose seeds are found in the marketed products. Greenhouses at Washington and cultural grounds at Arlington, Va., are at his disposal; not content with these facilities alone, he has been known to carry off material for propagation to his own farm in Maryland, presumably to watch it grow at night. His is a well-known figure at the important Port Laboratories of the Bureau of Chemistry. During the spring of 1922 he investigated at first-hand that little-known source of American crude drugs—the Blue Ridge. A European trip, from which he has just returned, has brought him into renewed touch wih foreign drug conditions.

"Extra Governmental agencies of a scientific sort have profited by his abilities. He is the newly elected chairman of the Scientific

Section of the American Pharmaceutical Association and a member of the Association's Council. He has been for some year's Associate Referee on Drugs of the Association of Official Agricultural Chemists."

Professor Stanford is not satisfied to submit the usual desiccated life story of the scientific man, but enlivens his presentation by describing how agreeably surprised he was on his first visit to the headquarters of this pharmacognosist in Washington. Instead of the expected bewhiskered and solemn-visaged recluse he finds this ————, but let Professor Stanford tell his own story:

"Above an official desk, furnished, indeed, with the strange apparatus and surrounded with the bulky tomes of our supposititious recluse of science, we find a beardless, almost boyish face, a quick dark eye, which lights as soon at a spark of humor as at a new histological discovery. Rising, with a quick, firm handclasp, this man reveals, to his intimates at least, a range of interest abstruse enough on the one hand to command the respect of the venerable professor we had envisaged, but roaming far enough on the other to include the more human, gentler arts of lyric and harmony with a more than amateur grasp. If we arrive on B Street too late for an interview—though his day is never bounded by merely legal hours—we may see his disappearing form, very briefly, in a 'well-known light car,' intent only on 'making' the red-clay roads of Maryland in time to function as an officer of his county council. Or perhaps the speeding vehicle may be hastening him to an evening row with his children on the Placid Potomac which borders his farm. For Arno Viehoever, scientist, Federal officer, musician, still finds time, or creates it, to function as an active American citizen and an enthusiastic American father."

A partial list of Dr. Viehoever's contributions to the literature is appended and is a revelation in its expansiveness and in the diversity of fields which it covers:

"On the Determination of Small Quantities of Hydrocyanic Acid." (Co-author.) *J. Am. Chem. Soc.*, *37*, No. 3, 1915, 601-607.

"Cyanogenesis in Plants. Studies in Tridens Flavus (Tall Red Top)." (Co-author.) *J. Biol. Chem.*, *25*, No. 1, 1916, 141-150.

"Sensitivity of Some Commercial Litmus Papers." (Co-author.) *J. Am. Pharm. Assoc.*, *9*, No. 6, 1916, 599-602.

"A Saponin From *Yucca Filamentosa.* (Co-author.) *J. Biol. Chem., 28,* No. 2, 1917, 437-443.

"On the Detection of Mold in Drugs, Foods and Spices. With Special Reference to a Specific Stain." *J. Am. Pharm. Assoc., 6,* No. 6, 1917, 518-524.

"Chemistry of the Cotton Plant. With Special Reference to Upland Cotton." (Co-author.) *J. Agric. Research, 13,* No. 7, 1918, 345-352.

"Chemistry and Histology of the Glands of the Cotton Plant. With Notes on the Occurrence of Similar Glands in Related Plants." (Co-author.) *J. Agric. Research, 13,* No. 8, 1918, 419-435.

"Commercial Viburnum Barks and Preparations." (Co-author.) *J. Am. Pharm Assoc., 7,* No. 11, 1918, 944-952. (Received Ebert Prize.)

"Some Effects of the War Upon Crude Drug Importations." (Co-author.) *J. Am. Pharm. Assoc., 8,* No. 6, 1919, 459-471.

"The Pharmacognosy Laboratory—Its Activities and Aims." *J. Am. Pharm. Assoc., 8,* No. 9, 1919, 717-725.

"Acid-insoluble Ash Standards for Crude Drugs." (Co-author.) *J. Am. Pharm. Assoc., 8,* No. 9, 1919, 725-730.

"Chinese Colza—A Valuable New Oilseed." *Oil, Paint and Drug Reporter,* September 8, 1919, 53.

"Report on Medicinal Plants." *J. A. O. A. C., 3,* No. 3, 1920, 381-386.

(1) A Consideration of a Method for the Determination of Volatile Oil Found in True Mustard and Mustard Substitutes.

(2) A Brief Discussion of the Determination of Ethereal Oil in Drugs and Spices.

(3) The Adulteration of Crude Drugs and Spices.

"Report on Medicinal Plants." *J. A. O. A. C., 4,* No. 1, 1920, 149-155.

(1) A Method for the Determination of Volatile Oil in Mustard Seed and Substitutes.

(2) Methods for the Hydrolysis of Linamarin and the Subsequent Determination of Hydrocyanic Acid.

(3) The Effect of Abnormal Conditions on Trade in Crude Drugs.

(4) The Value of Weights of Unit Volumes in the Analysis of Crude Drugs and Spices.

"Relative Content of Volatile Oil and Ash in Sage Leaves and Stems." (Co-author.) *J. Am. Pharm. Assoc., 9,* No. 6, 1920, 563-567.

"Popular Names of Crude Drugs." *J. Am. Pharm. Assoc., 9,* No. 7, 1920, 671-676.

"Commercial Hydrastis (Goldenseal)." *J. Am. Pharm. Assoc., 9,* No. 8, 1920, 779-784.

"Studies in Mustard Seeds and Substitutes: I. Chinese Colza (*Brassica Campestris Chinoleifera,* Viehoever)." (Co-author.) *J. Agric. Research, 20,* No. 2, 1920, 117-139.

"Chinese Colza—An Adulterant of Mustard Seed. *J. Am. Pharm. Assoc., 10,* No. 1, 1921, 16-19.

"Domestic and Imported Veratrum (Hellebore), *Veratrum Viride* Ait., *Veratrum Californicum,* Durand, and *Veratrum Album L.*: I. Botanical Studies." (Co-author.) *J. Am. Pharm. Assoc., 10,* No. 8, 1921, 581-593.

"Fake Saffron." (Co-author.) *J. Am. Pharm. Assoc., 10,* No. 9, 1921, 671-674.

"In Memoriam: Ernst Schmidt, Past Master of Pharmaceutical Research." *J. Am. Pharm. Assoc., 10,* No. 12, 1921, 695-696.

"The Substitution of Convallaria Flowers for Chamomile." (Co-author.) *J. Am. Pharm. Assoc., 10,* No. 12, 1921, 937-938.

"Alkaloids in Rhizomes and Roots of Ipecac." (Co-author.) *J. Am. Pharm. Assoc., 10,* No. 10, 1921, 763-766.

"Robusta Coffee." (Co-author.) *J. A. O. A. C., 5,* No. 2, 1921, 274-288.

"Report on Medicinal Plants." *J. A. O. A. C., 4,* No. 3, 1921, 409-415.

(1) Work Concerning New Sources of Supplies or Proper Substitutes for Drugs Not Now Obtainable.

(2) Value of Volume Weight Determinations in the Analysis of Crude Drugs and Spices.

(3) Value of Micro-Sublimation in the Analysis of Plant Products.

(4) Condition of Domestic and Imported Drugs.

"Report on Medicinal Plants." *J. A. O. A. C., 5,* No. 2, 1921, 155-163.

(1) Detection of Molds in Drugs, Foods and Spices, by Means of the Chitin Test.

(2) Identification and Differentiation of Plants and Plant Products by Means of the Pollen Grains.

(3) Value of Weights of Unit Volumes or the Specific Weight of Crude Drugs and Spices.

(4) Important Adulterants and Substitutes of Crude Drugs and Spices.

"Domestic and Imported Veratrum (Hellebore), *Veratrum Viride* Ait., *Veratrum Californicum* Durand, and *Veratrum Album L.:* II. Chemical Studies." (Co-author.) *J. Am. Pharm. Assoc., 11,* No. 3, 1922, 166-174.

"Problems, We, as Officials, Have in Common With the Trade." *J. Am. Pharm. Assoc., 11,* No. 8, 1922, 592-595.

"Report on Medicinal Plants." *J. A. O. A. C., 5,* No. 4, 1922, 553-563.

(1) Volume Weight Determinations of Crude Drugs and Spices.

(2) Micro-Sublimation of Plant Products.

(3) Identification of Crude Drug Substitutes.

"A Saponin From *Agave Lechuguilla* Torrey." (Co-author.) *J. Biol. Chem., 52,* No. 1, 1922, 335-347.

"Interesting Substitutes for Food Products." *Amer. Food Journ., 17,* No. 1, 1922, 21-24.

"Report on Medicinal Plants." *J. A. O. A. C., 6,* No. 4, 1923, 473-478.

(1) Sublimation of Plant and Animal Products. Third Report.

(2) A New Sedimentation Tube and Its Use in Determining the Cleanliness of Drugs and Spices.

"Domestic Sources of Cantharidin: I. *Macrobasis Albida* Say." (Co-author.) *J. A. O. A. C., 6,* No. 4, 1923, 489-492.

"Two Months Abroad to Study Crude Drugs and Spices." *Food and Drug Review, 7,* No. 2, 1923, 35-36.

"New Sources of Santonin." (Co-author.) *J. Am. Chem. Soc.,* Vol.

ABSTRACTED AND REPRINTED ARTICLES

THE HISTORY OF COD-LIVER OIL AS A REMEDY.*

Ruth A. Guy, M. D.

The revival of the use of cod-liver oil in therapeutics and the newly awakened interest concerning its action have stimulated this inquiry into the history of its employment in medicine.

The use of fish oils in medicine is mentioned by Hippocrates, and Pliny writes that the oil of the livers of the dolphin was used for chronic eruptions of the skin, not only as an external application, but also internally. No definite mention of the oil from the various species of *Gadus* is found in Greek and Roman literature (Bennett). Apparently, however, cod-liver oil has been used by the fisherman along the coasts of northern Europe for many years. It is stated that, in the Island of Shetland and the north of Scotland generally, the liver of the cod has long been considered a special delicacy, and hence is given to invalids and people in poor health, particularly for "old pains," and that the fresh oil from the livers was used as butter and considered especially delicious. The use of cod-liver oil by physicians was first recorded in England by Darbey at the Manchester Infirmary in 1789, who wrote:

> A woman who laboured under the most excruciating rheumatism and was an outpatient of this infirmary, being advised to rub her joints with the oil, was induced to take it at the same time internally. A few weeks restored her to the use of her limbs, and she was cured. However, little attention was paid to this case, as it was supposed that the alteration of the weather, and the medicine she had before taken, had caused the cure. About a twelvemonth afterwards, her complaints returned with double violence, and the same remedy restored her to health again. Encouraged by this second recovery, Dr. Kay (1766), one of the physicians to the infirmary, prescribed it for other patients, in similar cases; and it answered his most sanguine expectations. Since then, it has been used by the other physicians with the greatest success.

*From the *American Journal of Diseases of Children*, August, 1923.

The popularity of cod-liver oil for chronic rheumatism became so great at the Manchester Infirmary that "near a hogshead annually" was used there. In 1771, Percival entered it in the British Pharmacopœia; later, in 1790, he wrote thus of its effect in chronic rheumatism:

> While I was one of the physicians to this charity [Manchester Infirmary], I had the fullest evidence of the successful exhibition of cod-liver oil, in various maladies, of the class above described, which had resisted other powerful modes of treatment. And I frequently compared its operation with that of gum guaiacum, by prescribing each, at the same time, to different patients in similar circumstances. These trials almost always terminated in favour of the oil; and the patients who took guaiacum, by conferring with their fellow-sufferers, were sometimes so sensible of making a slower progress toward recovery, as to request a change of one remedy for the other.

The observations of Dr. Bardsley (1807) concerning its employment at the Manchester Infirmary also are interesting.

> From long and repeated experience, I am enabled to speak of it as a medicine of efficacious, but limited powers. In some instances, where every other means has proved unsuccessful, it has operated in a manner so decidedly beneficial as to excite astonishment. But, on the other hand, it has frequently failed in some of the mild and more common rheumatic affections. The circumstances under which I have found it most advantageous, when used both externally and internally, are the following: 1. In the chronic rheumatism of elderly persons, where the muscles and tendons have become rigid, and the joints nearly inflexible, in consequence of the disease having been brought on by excessive labour, hard fare, dampness, and cold. 2. In women whose constitutions have been worn out by repeated rheumatic attacks after parturition, and more especially in the decline of life. I have seen a few patients recover entirely by the exhibition of the oil; who, on their admission into the house, were unable either to preserve the body in an erect posture, or support its weight on the lower extremities.

It seems very probable that some of the cases of "rheumatism" in which the effects were "so beneficial as to excite astonishment" were osteomalacia.

Although undoubtedly cod-liver oil continued to be a family remedy in different parts of the country, apparently it was little

used by physicians during the next thirty years. At any rate, in the English medical literature of that period, no further mention of it has been found until its revival in 1841 by Bennett, who had travelled in Germany and had observed its employment there.

In 1822, the Society of Science and Arts of Utrecht made the chemical and therapeutic properties of cod-liver oil the subject of a prize essay. Apparently, therefore, its use in scrofula and rickets was known to the Dutch medical profession at that time. Bennett states that in Holland it had obtained a wide reputation for the cure of rickets long before its remedial properties were acknowledged by medical men.

In the same year (1822), Schenck published the first German article on cod-liver oil as a therapeutic agent. This article deals with the details of a number of cases of rheumatism and gout which were greatly relieved or entirely cured by cod-liver oil.

Schütte, in 1824, published the first definite case histories of rickets cured by cod-liver oil, stating that he had used it for twenty-five years. The cases he cited were in children, from three to five years of age, and unable to walk, who were cured in from five to nine weeks. In each instance, the parents or relatives had prescribed the remedy. He definitely attributed to Percival the introduction of cod-liver oil into medical literature.

In 1826, Schenck reported its successful use in four cases of rickets. He wrote:

> I am able to recall that my venerated teacher Michaelis, in Marburg, recounted to us in his lectures in special therapy, under the chapter on chronic rheumatism, that he had during his stay in England at the hospital in Manchester seen cod-liver oil used with striking success against chronic rheumatism.

From this time on, numerous German authors wrote on the subject, and cod-liver oil became very generally used throughout Germany for rheumatism, gout, and rickets, and hence for scrofula and tuberculosis.

Even before the middle of the century accounts of failure and of contaminations and substitutes for real cod-liver oil appeared in the literature. So great was the demand that all sorts of substitutes were used. In one instance a substitute was even

flavoured with decayed herring to give the characteristic offensive taste and smell.

The introduction of cod-liver oil into France, which came a few years later than in Germany, is described by Trousseau:

> The manner in which M. Bretonneau, of Tours, was induced to give the oil in this disease deserves notice. He had treated the rachitic child of a rich Dutch merchant with preparations of iodine and other means for some time without success. He was then told by the father that the elder children had previously suffered under the same malady, and had been cured by cod-liver oil, which in Holland was a popular remedy. Bretonneau gave the same substance to his young patient, and was much struck with the very rapid and successful result which followed. He commenced making researches with it on other patients, and it was only then that he learnt for the first time what had been written by the German authors on this subject. He has since given it extensively in rachitis, with the happiest results. This fact was communicated to the Société de Médicine de Paris, in 1837, by M. Roche.

In 1836 de Villards published the first article in France on its therapeutic value, but it was not until Trousseau, about the middle of the century, taught of its use and related the experiences of his celebrated colleague Bretonneau that it became generally known and recommended.

In each country the experience was the same: Cod-liver oil was used by the fishing people and peasantry; then accidentally observed by some physician, tried by him, and so made known generally to the profession. At first it was used in chronic rheumatism and gout; then, naturally enough, in other bone and joint diseases, notably rickets and osteomalacia (which was considered closely allied to gout); then in scrofula, because of its supposed identity with rickets, and finally in other forms of tuberculosis. It is interesting that its use in tuberculosis should have been by the way of rickets and gout.

It is interesting, too, that, despite the fact that it was so effective in rickets and despite the fact that this efficacy had been observed and carefully recorded by reputable and well-known medical writers, it should have fallen into such widespread disuse. It is well recommended and reported as late as the middle of the nineteenth century; but late in that century and early in this one the textbooks of pharmacology all speak of cod-liver oil as being useful

in tuberculosis and rickets because, and only because, it is an easily digested and easily assimilated fat (Potter, 1902; Stevens, 1903; Penzoldt, 1904; Hare, 1907; Cushny, 1911 and 1915; Sollmann, 1917). At the same time appear numerous notes as to the detection, in samples then on the market, of adulteration or substitution of other oils, and also clinical reports both of success and of failure in its therapeutic use. Heubner, Salge, Baginsky, Biedert, and Fischl found it of no use in rickets. Vierordt, Stöltzner, and Finkelstein maintained a vigorous defence of it, although they emphasized the importance of combining it with phosphorus. From 1908 to 1912, Schabad published the much-discussed metabolism experiments, which indicated a specific effect in rickets not produced by other oils. He pointed out certain pitfalls in relation to latent period and dosage. In 1910, Rosenstern wrote: "Cod-liver oil is in the forefront of children's remedies. For long it has been struggling against the scepticism of exact science." He reported cures in cases of early rickets and tetany with cod-liver oil alone, and considered the effect specific. Czerny, in 1912, asserted most positively that its only effect was due to its easily assimilated fat. No definite reports of its failure in actual use appeared in the literature in this country or in England. However, pharmacologists and chemists were convinced that its action was in no way specific, and certain noted pediatricians ,whose influence was widespread, taught that it was of no particular value. In the 1901 edition of Rotch's "Pediatrics," he says:

> The treatment of rachitis is essentially dietitic and hygienic. The infants should be kept in the open air as much as possible, and should live in rooms accessible to sunlight. There does not seem to be any drug which produces specific effect upon the osseous changes which take place in rachitis. Phosphorus is considered by some observers to be a valuable adjunct in the general dietitic and hygienic treatment, but, according to our experience at the children's hospital, it has not proved to be of any special benefit.

He makes no mention of cod-liver oil.

Still, in his textbook, in 1912, he notes the use of cod-liver oil and gives the dosage, and adds:

> There seems to be no specific virtue in cod-liver oil, any other oil will do equally well, provided it can be taken without disturbing digestion or causing nausea by its taste. At one time

we used, at the Children's Hospital, Great Ormond Street, olive oil and pilchard oil and cotton-seed oil, made into as palatable an emulsion as possible, and these seemed to be as useful as cod-liver oil, except that they were more apt to cause nausea or digestive disturbance.

Henoch, 1882; Meiggs and Pepper, 1886; Starr, 1894; Holt, 1896; Kerley, 1907; and Fischer, 1907, in their general textbooks, advised the use of cod-liver oil, and many physicians were impressed with its obvious benefit in rickets, and continued its use. Recently, well-controlled experiments both in the rat and in the human infant have demonstrated beyond criticism the efficacy of cod-liver oil in the cure and prevention of rickets, and attention may now be directed to the mechanism which brings about this effect.

SO-CALLED "IMPROVED" ETHERS.*

Claim that Pure Ether Has No Anesthetic Properties, Without Foundation.

Since the use of ether for anesthesia was demonstrated in 1846 there have been many investigations of its composition in relation to its actions. The generally accepted view has been that the anesthetic action of ether is due to the ether (diethyl oxid) itself, although at various times during the first five decades of its employment assertions were made—without substantiating evidence—that certain impurities enhanced its anesthetic value.

In 1919 Cotton[1] declared that, as a result of certain experiments, ethyl ether, specially purified, "was not a good anesthetic and that real anesthesia could not be obtained unless it [ether] contained some potent synergist." He then announced that he had prepared a superior product, which became known as "Cotton Process Ether."

At that time the exact composition was not given but some time later, the manufacturer who placed the product on the market, E. I

*Reprinted from *Journ. Amer. Med. Assoc.*

[1] Cotton, J. H.: "Cotton Process Ether and Ether Analgesia." *Am. J. Surg., Anesthesia Supplement,* April, 1919, p. 34.

Dupont de Nemours & Co., Inc., stated [2] that the composition was highly refined diethyl oxid $(C_2H_5)_2O$, plus approximately two volumes of ethylene (C_2H_4), one-half volume of carbon dioxid (CO_2) and 1 per cent. by weight of ethyl alcohol. The firm also signified its intention of submitting the product to the Council on Pharmacy and Chemistry, which it did two years later. Since that time the company, apparently, has endeavored to obtain sufficient evidence for claims of superiority, but so far these have not been presented and confirmation of Cotton's claims is lacking. It is but fair to say that the Dupont Company has not been actively "pushing" the product during the past two years.

Wallis and Hewer of England have also recommended a new general anesthetic. They, too, declare [3] that pure ether possesses practically no anesthetic properties. The composition of the Wallis and Hewer product has been vaguely claimed to be purified ether to which is added, in unspecified amounts, a mixture of ketones (identified only as comprising those in the middle of the series) which have been treated previously with carbon dioxid and ethylene. The product has been placed on the market under the name "Ethanesal." It received some endorsement, especially from Dr. H. E. G. Boyle of London who made it the subject of addresses on anesthesia before medical audiences in this country.

The claim that pure ether is devoid of the usual anesthetic attributes seemed so out of accord with the understanding of ether anesthesia that it was not surprising that other investigators took up the problem. Thus it was that over a year ago Bourne and Stehle [4] showed that ether prepared in a way to exclude impurities such as are ordinarily present possesses the usual anesthetic properties. As for "Ethanesal," Henry Robinson [5] states in his recent textbook:

[2] "Cotton Process Ether." *J. A. M. A.* 74: 1474, 1920.

[3] Wallis, R. L. McK., and Hewer, C. L.: "New General Anesthetic, Its Theory and Practice." *Lancet* 1: 1173, 1921.

[4] Stehle, R. L., and Bourne, W.: "The Anesthetic Properties of Pure Ether." *J. A. M. A.* 79: 375, 1922.

[5] Robinson, Henry: "Hewitt's Anesthetics and Their Administration." New York: *Oxford University Press,* 1922.

"I have been unable to discover any advantage possessed by this anesthetic over ether; and in particular I believe that so far from being less liable (as is claimed) to cause vomiting, ethanesal is actually more often followed by vomiting than ether itself. Ethanesal is considerably the more expensive of the two."

Of particular scientific interest is the painstaking investigation recently reported by Dale, Hadfield and King[6] made by them for the purpose of throwing light on the claim that pure ether has little or no anesthetic action. They also report the results of their examination of "Ethanesal." They first made a purified ether—absolute diethyl oxid—by a special method. This ether, which was free from aldehydes, ketones, acids, mercaptains, alcohol and all other known impurities, including ethylene, was first carefully tested in the laboratory on a series of cats. Induction of anesthesia occurred smoothly and with a rapidity at least equal to that normally seen when ordinary good anesthetic ether is administered. Such difference as was observable could be satisfactorily attributed to the smaller amount of pharyngeal and tracheal secretion invoked, the pure ether being distinctly less irritant than the specimens of ether sold for anesthetic purposes. This absence of irritation not only facilitated induction, but enabled the anesthesia to be maintained with a smaller quantity of the ether. As a result of their experiments, the authors believe that the purer the ether, the more easily and smoothly can anesthesia be induced and maintained.

When this pure ether was used for patients requiring anesthesia with ether for surgical operations, the results, like those obtained in experiments on cats, were decisive in favor of perfectly pure ether. The after-effects were no worse than those usually following anesthetic ether. During the administration the tendency to coughing and salivation appeared to be less than usual. In all cases the surgical anesthesia was complete and no complaint was made of rigidity. These experiments appear to prove beyond doubt that chemically pure ether is an anesthetic, at least as satisfactory and effective for the human subject as the best ethers usually sold for that purpose. In the opinion of these investigators efforts to improve the properties of ether, as an anesthetic for ordi-

[6] "Anesthetic Action of Pure Ether." *Lancet* 1: 5192 (March 3) 1923.

nary use, can be most profitably directed to the discovery of methods for rendering and keeping it free from the irritant impurities

The experiments with "Ethanesal," made by Dale, Hadfield and King, failed to afford any evidence of an anesthetic potency which is not satisfactorily accounted for by that of the purified ether, which is its main constituent. Several samples of "Ethanesal" were submitted to fractionation. The samples contained 95.5 per cent. ether, 4 per cent. of normal butyl alcohol, and 0.5 per cent. of a mixture of ethyl alcohol and an aldehyde, and possibly traces of other substances. This analysis showed a composition which differs from the claims. These differences were called to the attention of the manufacturers of "Ethanesal" who stated that normal butyl alcohol should not be a constituent of "Ethanesal," and that its presence in the samples examined must have been due to an error. The authors claim they are left in a state of complete uncertainty as to whether any of the numerous published clinical observations of the action of "Ethanesal" were carried out with ether containing genuine ketones (as claimed by the manufacturers) or with ether containing normal butyl alcohol (as found by the investigators) of which some portion had been oxidized to butylic aldehyde. Meanwhile, in view of their failure to detect any real difference between the action of "Ethanesal" and that of pure ether (either separated from it, or prepared independently) they feel justified in requiring further proof before admitting that the nature of the added constituent could make any serious difference.

Thus the work of Dale, Hadfield and King gives no support to the statements that pure ether is devoid of anesthetic action, and that the activity in this direction of ordinary ether is due to impurities. On the contrary, their work shows that the anesthetic action of ether is improved by purification. As an anesthetic, the purest ether is the best. Furthermore, the work of these men indicates that there is no evidence to warrant attributing the anesthetic properties of "Ethanesal" to any other constituent than the ether.

The work of Stehle and Bourne in Canada and of Dale and his co-workers in England demonstrates anew that, notwithstanding the claims of the proponents of the so-called improved ethers the theory of ether anesthesia is still unchanged.

SCIENTIFIC AND TECHNICAL ABSTRACTS

(Abstracts of Papers Read at the 1923 Meeting of the American Chemical Society.)

BUTESIN PICRATE, A NEW TYPE OF ANESTHETIC-ANTISEPTIC.—F. K. Thayer.—Butesin Picrate is the picric acid salt of butyl para-aminobenzoate. There is combined in a definite chemical compound both antiseptic and anesthetic action. In an aqueous solution with a concentration of 1 part in 1400 it produces immediate and complete anesthesia upon the eye which lasts from 10 to 20 minutes. It exerts antiseptic action and, in many cases, germicidal action against various common bacteria, in concentrations of 1 :400 to 1 :800.

Butesin Picrate is non-toxic and not irritating to the most sensitive surfaces. Incorporated into an ointment it is useful in the treatment of painful, denuded skin areas, particularly in cases of burns.

THE ANTISEPTIC ACTION OF THE ZINC CHLORIDE SALT OF ANILINE.—J. W. Howard and F. D. Stimpert.—This salt was prepared by combining zinc chloride and aniline in molecular quantities and extracting the reaction mixture with boiling 95 per cent. alcohol. Softens at 230° C., melts at 255° C. Solubilities:—at 20° C., 0.64 grms. in 100 cc. H_2O; 0.87 grms. in 100 cc. 0.4 HCl; 0.066 grms. in 100 cc. 95 per cent. alcohol. V. slightly sol. in CS_2, $CHCl_3$, C_6H_6, $(C_2H_5)_2O$. More soluble in CH_3OH and acetone. Slowly decomposed by 3N Na_2CO_3, readily by 1N NaOH or boiling H_2O.

Studies on Staphylococcus aureus indicate that aniline has about five times the disinfectant power of $ZnCl_2$. The salt $(C_6H_5NH_2)_2$ $ZnCl_2$ in 0.6 per cent. solution retards growth up to 25 minutes and will destroy in 30 minutes. Compared with aniline and zinc chloride of the same concentration, it shows a stronger antiseptic action.

DETERMINATION OF IODIN IN NATURAL WATERS.—J. F. McClendon.—The method of reduction of iodate to iodide and the oxidation of iodide to iodin, shaking this out with carbon-tetra-

chloride and determining colorimetrically is adapted to quantities of .001 milligrams or greater by the use of a Bausch and Lomb colorimeter, cups holding 1 cc. at 2 cm. depth. Water residue is first ignited in pure oxygen in a silica combustion tube with the end bent down into KOH solution.

DETERMINATION OF IODIN IN LARGE QUANTITIES OF FOODSTUFFS.—J. F. McClendon.—The method is similar to the method for water except that the sample is burned in two stages. The first stage in an apparatus similar to the silica tube described before, but large enough to burn several kilograms. KOH solution is evaporated down and together with the ash is reburned in the smaller tube and analyzed as in the preceding.

THE LOWEST TEMPERATURE YET OBTAINED.—In a communication in the *Transactions of the Faraday Society* (1922, xviii, 145), Dr. Kamerlingh Onnes, the Dutch chemist who has been especially distinguished for low temperature investigations, gives in detail some results recently obtained by him, in which the temperature of liquid helium has been brought to within less than a degree of the absolute zero. The liquefaction of helium having been successfully accomplished, efforts were made to freeze it. The method adopted is that of evaporation under reduced pressure. The initial procedure is with liquid hydrogen. A large volume of this was made, incidental to which operation the preparation of about twice the volume of liquid air was necessary. The helium was converted into a liquid and then allowed to evaporate under favorable conditions, the course of the evaporation being closely watched with care not to cause any elevation of temperature in the liquid. No evidence of solidification was obtained, the liquid preserving its mobility throughout the procedure. Onnes expresses the view that in the experiment he had reached a temperature within less than one degree of the absolute zero, the point being taken as 0.82° K. As a conservative estimate he prefers to give the temperature at some hundredths of a degree below 0.9° K. (K. is the symbol for Kelvin degrees, centigrade degrees with the zero at —273° C., which is regarded as the absolute zero). Onnes considers it possible that

helium may not solidify at the absolute zero. However, he calls attention to the fact that other problems in science have been regarded as unsolvable, and yet have been fully solved. Even in this field, the study of which was begun by Faraday, who showed the possibility of liquefying many of the common gases, there was at first a disposition to place certain gases in the "permanent" list, regarding them as incapable of liquefaction, but all these have yielded to patient investigation.

H. L.

DIETHYL SULFATE: A NEW ETHYLAT'NG AGENT.—For some time past Mellon Institute of Industrial Research, University of Pittsburgh, Pittsburgh, Pa., in connection with the work of the Multiple Industrial Fellowship sustained by the Carbide and Carbon Chemicals Corporation, 30 East Forty-second Street, New York, N. Y., has been making a thorough investigation of the properties and uses of diethyl sulfate as a general ethylating agent. Mr. A. R. Cade, an Industrial Fellow of the Institute, under whom the greater part of the work on this subject has been carried out, has published recently in *Chemical and Metallurgical Engineering* a report of the findings of this investigation, which report shows diethyl sulfate to be a most satisfactory general reagent for introducing ethyl groups into organic compounds. Mellon Institute will be pleased to furnish samples of this material to anyone interested, and Mr. Cade will correspond gladly with anyone who desires further information upon this subject. Reprints of the article referred to above may be obtained by writing to Mr. Cade at the Institute.

SIMILARITY OF CHEMICAL TERMS AS A CAUSE OF ACCIDENTAL POISONINGS.—Attention was called in the July issue of this journal to a fatal case of poisoning by mistaking barium sulphide for sulphate. The account was taken from the *Schweiz. Apoth. Zeit.*, and a subsequent number gives some information as to the trial of the case. The attorney for the defendant spoke sarcastically of "Das Spiel mit Buchstaben," "letter-play," in which chemists indulge, evidently referring to the fact that though barium sulphate and barium sulphide are very different substances, their names are quite similar and rather easily confused by persons not well trained in chemistry.

The similarity betwen "sulphite" and "sulphide" is still closer, especially in ordinary pronunciation, though the correct pronunciation of "sulphide" is with the short "i," rhyming with "bid" and not with "bide." The suggested new spelling for chemical terms in which the silent final "e" is dropped when it does not render the preceding vowel long, would lessen the confusion, for there would be no difficulty in distinguishing the "sulphid" from the "sulphite," and the difference in spelling would aid. The Swiss journal just quoted, has a note on these confusing terms, which are in some respects more troublesome in German than in English, and are often misleading in translation. Thus kalium chloratum is potassium chloride; kalium chloricum, potassium chlorate. It was stated many years ago that the introduction of potassium chlorate into medicine—probably one of greatest absurdities in modern therapeutics—was due to mistranslation of the German term, the original suggestion being the potassium chloride, but taken for chlorate on account of the form of the word. The Pharmacopœias have avoided one source of danger, in distinguishing the two mercury chlorides as "mild" and "corrosive," respectively.

The problem is one of much importance, and it is difficult to see any way to solve it. The "letter-play" may have to continue among chemists, for there is no likelihood that they will return to the old alchemical names, speaking of "vitriolated tartar," "sal prunelle," "spirit of salt" and so on. An effort to eliminate the tendency to use methyl hydroxide as a substitute or adulterant of common alcohol has been made by avoiding all scientific use of such terms as "wood spirt," "wood alcohol," and using "methanol." This commendable suggestion should meet with general response among chemists and dealers in chemicals, that the dangerous terms should disappear promptly from use.

H. L.

MEDICAL AND PHARMACEUTICAL NOTES

A New Cause of Hay Fever.—Summarizing a careful and extended investigation, Dr. George Potts, Professor of Botany, Grey University College, Bloemfontein, South Africa, finds that hay fever in that district is due to the pollen of the pepper tree, *Schinus molle*

L. of the sumac family (*Anacardiaceae*). The tree is much cultivated for ornament and shade and notwithstanding the fact that it produces a sticky pollen, the dryness of the district during a large part of the year and the frequent winds cause a distribution of pollen grains in considerable abundance. Dr. Potts exposed plates coated with vaselin and found the *Schinus* pollen to be most abundant of the material other than common dust collected. He also found the pollen in the discharges from the mucous membranes of persons affected. As in other parts of the world many persons are not susceptible to the influence, but those who develop the disease often have it severely. The tree is dioecious, and it is recommended, as a preventive measure, that only a limited number of staminate trees should be cultivated. The fertilization is essentially by insect agency, as indicated by the character of the pollen. The flowers are visited by many flies as well as by wasps and bees. The flies are probably merely predatory, eating the pollen. It is generally believed that only plants producing dusty pollen and, therefore, wind-fertilized, will give rise to hay fever, but the extreme dryness and windiness of the climate in region of Bloemfontein causes an otherwise sticky pollen to be widely distributed. The grains average about 33 microns long by 17 broad, with a smooth surface. In shape it resembles a grain of wheat slightly truncated at each end. Dr. Potts, by his careful investigations, seems to have eliminated all other causes, and to have shown that the pollen of this tree is the cause of the fever. The paper is published in the *South African Journal of Science* (1922, XIX, 146). The journal is the annual report of the South African Association for the Advancement of Science. Interesting evidence of the British-Portuguese entente is the printing of two papers in Portuguese and the fact that the 1922 meeting was held at Lourenco Marques. The headquarters of the Society are, however, at Johannesburg.

H. L.

Active Constituents of Rhubarb.—The cessation of the importation of Chinese rhubarb into Germany during the war led to renewed attention being paid to the cultivation of *Rheum palmatum,* Linn., and *R. officinale,* Baill., in Europe and particularly in Germany. The seeds of the former plant were obtained for this purpose from Prof. Tschirch in Bern, and the cultivation of both

species was prosecuted with great zeal by Prof. Ross, of Munich. Tschirch had come to the conclusion that the rhizomes of *R. palmatum* and *R. officinale* obtained from plants cultivated in England and France were not equal to the Chinese drug and were chemically of less value; this he ascribes to the fact that in China the plants grow at an altitude of 12,000 to 14,000 feet. Ross cultivated the plants at more than 100 localities in Germany, and found that, contrary to Tschirch's opinion, the plants did not thrive so well at altitudes between 2000 and 3000 metres as they did at lower heights. At 1800 metres they grew slowly; cultivated plants always yielded a good drug. Both Ross and Tschirch gave the preference to *R. palmatum,* as that is the species that yields the most valuable commercial rhubarb (Shensi), grows quicker, and is easily distinguished from *R. rhaponticum,* Linn. Semmler grew the same species in Russia, and found that the plants yielded the best drug when three or four years old, and that in respect of the amount of oxymethylanthraquinones present the cultivated drug was not only equal but even superior to the best Chinese rhubarb. The valuation of rhubarb as at present carried out depends upon the determination of the extract, ash, and percentage of oxymethylanthraquinones. As regards the extract and oxymethylanthraquinones, the author found that the roots of plants cultivated near Munich contained appreciably more than the rhizomes, and that therefore the separation of the roots and even the parings of the rhizomes were a waste of material. *R. officinale* was in both respects better than *R. palmatum.* The percentage of oxymethlyanthraquinones may be determined colorimetrically, spectroscopically or gravimetrically, but the real value of a rhubarb depends upon its activity rather than upon any theoretical considerations. When put to the practical test no difference could be detected between the two species cultivated by the author when doses of 1 gm. were administered. This is, however, too large a dose. It appears that the percentage of anthraquinone derivatives present is not in direct proportion to the activity of the drug. *R. palmatum* contains appreciably less anthraquinones than *R. officinale,* but in activity the former far surpasses the latter. *R. palmatum* with 2.268 per cent. of anthraquinones was much more active than *R. officinale* with 3.937 per cent. There is therefore undoubtedly some difference in the active constituents of these two drugs. Possibly an explanation is to be found in the fact that Eijken found no emodin in the rhizomes and roots of *R. officinale*

cultivated in Bern. Powdered *R. palmatum* was boiled with dilute sulphuric acid and chloroform under a reflux condenser for two and a half hours (as is done in the determination of the oxymethylanthraquinones) and the chloroformic solution of the oxymethylanthraquinones separated. The extracted powder, when tested for its therapeutical action, was found to have just the same action as it had before extraction. As emodin is difficultly soluble in chloroform, it may be assumed that a considerable proportion of that present in the original drug was left in the powder after extraction. The result of this experiment throws much doubt on the reliability of the method of estimating the activity of rhubarb by determining the percentage of oxymethylanthraquinones obtainable from it. These results were confirmed by exhausting powdered rhubarb with chloroform, which removed the free oxymethylanthraquinones, then boiling with dilute sulphuric acid and chloroform, separating the chloroformic solution, washing the residual powder with water until free from oxymethylanthraquinones (which occupied several days), and then drying. The powder thus exhausted acted as a satisfactory laxative with four persons out of the five on whom it was tried. Although these experiments, owing to the small number of persons on whom they were tried, are not conclusive. they indicate that the determination of the oxymethylanthraquinones in rhubarb is solely of theoretical interest.—L. Kroeber (*Schweiz. Apoth. Ztg.*, Vol. 61, p. 221).

Pre-Professional Preparation.—"There is something," said a cynical Frenchman, "in the misfortunes of our best friends that does not wholly displease us." "Misery loves company" is a sort of correlative proverb. At any rate, the faculties of American professional schools, especially those of medicine and pharmacy, may be interested in the struggles of other nations with problems of preliminary education for entrance into such schools. By direction of the educational authorities of Switzerland, a commission has formulated three types of preparatory education, satisfactory completion of which will entitle the student to enter not only the medical and pharmaceutical courses, but the polytechnic as well. The general character of this preparation is as follows:

A. Classical: including Greek and Latin;

B. Semi-classical: Greek being replaced by English or Italian;

C. Modern: Modern languages only included.

Much opposition has been developed among medical, dental, pharmaceutical and veterinary faculties against the abandonment of the classical courses. The polytechnic faculties doubtless feel their withers unwrung, as their courses have nowadays almost nothing to do with classical education. Instead, mathematics and physics are to the fore. A reading knowledge of French and German is undoubtedly necessary to the proper practise or teaching of any department of engineering, physics or chemistry. As a result of the strenuous opposition to the type C course as preliminary to the medical and allied schools, it has been decided to leave to those schools the determination of which types they will regard as equipping the student properly and the polytechnic schools will be given the same privilege. It is likely that the latter will select type C. The end is not yet. It seems certain that a rapid disintegration of classical education is occurring. The "dead languages" are losing ground, especially in the United States, in which the demand is loud for "practical" training. Yet the classical tongues are the source of our language, both as to the mass of ordinary words and almost wholly as to the technical terms, and ignorance of the elements of them is surely a handicap for the student in most sciences.

H. L.

Poisoning by Cocklebur.—The well-known and unsightly species of *Xanthium* have been generally considered mere nuisances, but it appears that one species at least has decidedly poisonous properties in the early stages of its growth. For some years complaints have been made to the United States Department of Agriculture concerning stock-poisoning said to be due to a species of cocklebur. Messrs. Marsh, Roe and Clawson, of the Department, undertook a careful investigation and have given their results in Dept. Cir. 283.

The species investigated was *Xanthium echinatum Murr.*, which is found mostly towards the western section of the country, and grows in moist places. It appears that in the cotyledon stage a distinct and active poisonous principle exists, but the mature plant does not seem to be harmful. The seed vessel usually contains two seeds, only one of which is likely to sprout the year after the fruit is dropped. Therefore, although the plant is annual, the second year growth must also be looked after. The fatal dose of the raw plant

is about 24 ounces to 100 pounds of the animal, but most animals. especially pigs, are apt to die if sickened by the material. It has been found that fats are an antidote. Animals to which a fatal dose had been given were treated with bacon grease, lard and raw linseed oil and recovered. It was found by a stockraiser in New Mexico that liberal use of milk also prevented serious results. The nature of the poisonous principle has not yet been determined.

H. L.

NEWS ITEMS AND PERSONAL NOTES

PROFESSOR YOUNGKEN GOES TO MASSACHUSETTS COLLEGE.—Professor Heber W. Youngken, for many years a respected member of the Faculty of the Philadelphia College of Pharmacy and Science, has accepted the Chair of Materia Medica and Botany at the Massachusetts College of Pharmacy.

With him, into his new field of activities and usefulness, go the best wishes of his former comrades-in-service. The AMERICAN JOURNAL OF PHARMACY, likewise, takes this opportunity to extend to Professor Youngken, long an active member of its Publication Committee and a frequent contributor to its pages, its felicitations and an assurance that its pages are as ever open to his contributions.

AMERICAN PHARMACEUTICAL ASSOCIATION RESEARCH AWARDS.—At the seventy-first annual meeting, held recently in Asheville, N. C. the American Pharmaceutical Association made the following grants from its Research Fund for the year 1923-1924:

To E. Kremers and K. H. Rang, of the University of Wisconsin, for work on decolorized tincture of iodine and on such other preparations of the National Formulary as time permits, $250.

To W. J. McGill, of the University of Michigan, for work on the electrometric titration of alkaloids, $200.

These research grants are made annually by the American Pharmaceutical Association from the interest accruing from the A. Ph. A. Research Fund, which represents the profits accruing from the sale of the National Formulary.

POPULAR LECTURES IN BOOK FORM.—In the course of the next few weeks the Journal will have completed publication, in book form, of the Series of Popular Lectures presented during the past winter months at the College. These lectures cover a wide range of subjects and are given in a non-technical style, so that the lay reader can readily grasp the information as recorded. The book may be procured, by addressing this Journal and enclosing one dollar to cover cost of printing and mailing.

FREE PUBLIC LECTURE COURSE

1923—1924

Philadelphia College of Pharmacy and Science

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The lectures will begin at 8.15 P. M.

This is the third season of the effort of the Philadelphia College of Pharmacy and Science to contribute to the educational welfare of the community at large by means of a series of popular scientific subjects.

The lectures are delivered by members of the Faculty of the institution and are abundantly illustrated by experiments, lantern slides and specimens.

Those which have been presented during the past two seasons have been attended and enjoyed by many interested persons.

They are given in a form which is simple and understandable and which is of interest alike to the person who has been technically trained along particular lines and to the one who is simply interested in scientific subjects in general.

First Lecture. Thursday Evening, October 11, 1923

SOME NEWS FROM OUTER DARKNESS.

By Henry Leffmann, A. M., M. D.

Lecturer on Research, Philadelphia College of Pharmacy and Science; Hon. Professor Organic Chemistry, Wagner Free Institute of Science, Etc.

Light is generally understood to be that form of energy

which our eyes can detect, but it is now known that many similar forms exist that are invisible to us under ordinary conditions, but which produce striking effects and in some cases can be rendered visible. The lecture will present a brief explanation of these invisible forms and illustrate some of their actions, including the phenomena of fluorescence and phosphorescence.

Second Lecture. Thursday Evening, October 25, 1923.

WIRE AND WIRELESS TELEPHONY.

By George Rosengarten, Ph. D.
Assistant Instructor in Physics, Philadelphia College of Pharmacy and Science.

The relation of the subject of wireless to the other fields of physical research will be discussed in order to clear the air of the "wonders" of the new means of communication. Sound waves and electro-magnetic waves—their similarity and difference, together with some fundamentals of sound and electricity; nature of radiations of various wave lengths; radio transmission a development due to scientific research; the electron as a carrier of sound vibration.

Third Lecture. Thursday Evening, November 8, 1923.

THE GREAT AMERICAN RUBBER INDUSTRY.

By J. W. Sturmer, Phar. D.
Dean of Science, Philadelphia College of Pharmacy and Science.

By the aid of lantern slides and much illustrative material, the Story of Rubber will be told. The lecture will deal with the gathering of wild rubber in Central and South America, with the development and present importance of rubber plantations, with the processes of manufacture, and of vulcanizing, with particular reference to the newer advances in the procedure of making automobile tires, and of other rubber commodities which have come to be indispensable.

Fourth Lecture. Thursday Evening, November 22, 1923.

CHEMISTRY IN AND ABOUT THE HOME.

By Freeman P. Stroup, Ph. M.

Professor of Chemistry, Philadelphia College of Pharmacy and Science.

Chemistry and physics play a very much more important role in domestic life than most people realize. Without being conscious of it, the one who tends the fires, the genius who presides over the cook stove, and even the laundress, carry out processes which are generally essentially chemical and always involve the application of some one or more principles of physics. It is evident then, that the more the operator knows of the "why" of the things and the more nearly the work is done along scientific lines, the greater will be the degree of success attained. The lecturer will endeavor to present in non-technical language the principles underlying many everyday household operations, particularly of the kitchen, with the hope of being helpful to many who imagine that they "never could learn chemistry."

Fifth Lecture. Thursday Evening, December 6, 1923.

WATER—AQUA—H_2O.

By Ralph R. Foran, P. D.

Assistant Professor of Technical and Analytical Chemistry, Philadelphia College of Pharmacy and Science.

The ancient Greeks said that water was one of the four elements or forms in which matter existed. We know now that it is a chemical compound, but it is such a common substance that we give it little attention and only realize its importance in our scheme of existence when the supply is curtailed.

It is concerned in feast and famine, flood and drought, joy and misery, life and death.

The lecture, which will be illustrated, will consider water in its relationship to all of these, together with some of its scientific aspects.

Sixth Lecture. Thursday Evening, December 20, 1923.

IDIOSYNCRASIES, OR THE STORY OF A SNEEZE.

By Ivor Griffith, P. D., Ph. M.

Physiological Chemist, Stetson Hospital, Philadelphia, Assistant Professor in Pharmacy, Philadelphia College of Pharmacy and Science, Editor American Journal of Pharmacy.

The subject of the lecture will be hay fever, "the American Midsummer Madness"; its causative factors, modes of diagnosis and treatment—how the modern chemist picks the culprit pollen responsible for the sneezing fits and makes it turn about to cure the sickened victim. Other protein antipathies will also be discussed—Tabby, the cat, Dobbin the drowsy, or Fido the faithful—often the innocent cause of persistent protein asthmas. The lecture will be illustrated with lantern slides.

Seventh Lecture. Thursday Evening, January 10, 1924.

RADIATIONS.

By David Wilbur Horn, Ph. D.

Professor of Physics and Physical Chemistry, Philadelphia College of Pharmacy and Science, Professor of Inorganic Chemistry, Wagner Free Institute of Science.

Discussion of cathode rays and positive rays—emission of electricity by hot bodies. Photo electric effects. X-rays, alpha, beta, and gamma rays. Radio-activity. The electron theory of matter.

Eighth Lecture. Thursday Evening, January 24, 1924.

WHAT IS CHOCOLATE?

By E. Fullerton Cook, Ph. M.

Professor of Operative Pharmacy and Director of the Pharmaceutical Laboratory, Philadelphia College of Pharmacy and Science.

A romantic story, linked with the Spanish Conquest of Central America. This treasure has proved to be "living gold," one of the richest gifts of the Western Hemisphere to the world.

It combines remarkable qualities—a food, a confection, a cosmetic and a medicine.

Its modern cultivation, marketing and manufacturing, including its important place in candy making, will be profusely illustrated.

Ninth Lecture. Thursday Evening, February 7, 1924.

SUGAR AS A MEDICINE, FOOD AND POISON.

By Horatio C. Wood, M. D.

Professor of Materia Medica, Philadelphia College of Pharmacy and Science.

Although some of the European scientists in the first century were familiar with a substance "resembling salt and tasting like honey"—evidently our modern sugar—it was not for ten centuries later that it acquired any common use in Europe. In the 10th century it was introduced into medicine as a drug, and a century later was employed as a condiment and food. In the 14th century it sold at a price which would be equivalent in modern times to about two dollars a pound.

Sugar is one of the most concentrated foods in common use. It is, however, entirely lacking in body-building properties, useful only for its energy value. Contrary to common belief, sugar is not especially easy to digest. These and many other interesting points will be fully discussed.

Tenth Lecture. Thursday Evening, February 21, 1924.

SOCIAL INSECTS.

By Marin S. Dunn, A. M.

Assistant Professor of Botany, Philadelphia College of Pharmacy and Science.

The lecture will cover the following topics—the place of the insect in the animal kingdom, the White Ants (Termites), their origin, mode of living, etc., the Honey Bee, the Bumble Bee, the Social Wasp, the Ants, and a discussion on the in-

stinct, intelligence and rationality, with examples. The lecture will be illustrated by charts, drawings, lantern slides and microscopic slides. Specimens will also be presented.

Eleventh Lecture. Thursday Evening, March 6, 1924.

THE ROMANCE OF DRUGS.

Part I—Vegetable Drugs.

By Charles H. LaWall, Pharm. D., Sc. D.

Chemist to Food Bureau, Pennsylvania Department of Agriculture, Professor of Pharmacy, Philadelphia College of Pharmacy and Science.

Among the rarest and most valuable of the products of early commerce were vegetable substances used for remedial purposes. In many of these drugs the value was dependent upon superstition or occultism. Sometimes the medicinal property of a plant was determined by the fancied resemblance of one of its parts to an organ of the human body; others depended for their value upon imagined planetary influence and "every herb had a star bespoke." Many owed their sole value to the secrecy and mystery attending their origin. Jesuit's Bark, Sacred Bitters, Ordeal Bean, Divine Plant of the Incas—these are titles which are reminiscent of the days when intrepid explorers brought back the products of strange lands; when kings paid enormous sums for the secret of some wonderful remedy which usually lost its efficacy along with its mystery.

The tale is one is one which lends itself well to illustration, and lantern slides and specimens will be shown.

Twelfth Lecture. Thursday Evening, March 20, 1924.

SOMETHING ABOUT GASES.

By Frank X. Moerk, Ph. M.

Director of the Technical Chemistry Courses, Philadelphia College of Pharmacy and Science.

There are many facts which the general public should know about gases, facts which have bearing upon the health and com-

fort of man. Air and ventilation, heating and illumination, refrigeration and cold storage, preservation of foods, deterioration of foods, preparation of bread and cakes. The matter will be so presented that persons who have not had the advantage of a scientific education will be able to gain many interesting and important points.

Thirteenth Lecture. Thursday Evening, April 3, 1924.

OUR MINUTE ENEMIES AND HOW TO ROUT THEM.

By Louis Gershenfeld, B. Sc., Ph. M.
Professor of Bacteriology, Philadelphia College of Pharmacy and Science

What are germs and germicides? What are the characteristics of the commonly found insect pests? What are insecticides and deodorants? What should be employed and how can it be used to best advantage so as to get rid of insects and germs? All of these questions are being constantly asked before and during house cleaning. Answers to these as well as other interesting data will be discussed in this lecture.

Fourteenth Lecture. Thursday Evening, April 17, 1924.

THE DRUGS OF THE NORTH AMERICAN INDIAN.

By Heber W. Youngken, Ph. M., Ph. D.
Formerly Professor of Biology and Pharmacognosy and Director of the Botanical Gardens, Philadelphia College of Pharmacy and Science.
At Present Professor of Botany and Pharmacognosy in the Massachusetts College of Pharmacy.

A story of the drugs and medicines employed by the Indian tribes of North America from the time of its early settlement by the white man, the superstitions and ceremonies connected with their use and the influence of Indian ideas and methods upon the materia medica of the present day.

The lecture will be illustrated by an exhibit of Indian drugs.